# Antiretroviral therapy adherence among People Living with HIV accessing services at a primary health care facility in Livingstone, Zambia, during the COVID-19 pandemic

Cynthia Chilumwaya

Student Number: 4104957

# A mini-thesis submitted in partial fulfilment of the requirements for the degree

of Master in Public Health at the School of Public Health, University of the

Western Cape

# **UNIVERSITY** of the

Supervisor: Prof. Brian van Wyk

Date: 22.05.2023

# DECLARATION

I declare that *Antiretroviral therapy adherence among People Living with HIV accessing services at a primary health care facility in Livingstone, Zambia, during the COVID-19 pandemic* has not been submitted for any degree or examination at any other university and that all the sources I have used have been indicated in text and acknowledged in the references section.

#### Full Name: Cynthia Chilumwaya

### Date: 22.05.2023





UNIVERSITY of the WESTERN CAPE

# **ACKNOWLEDGEMENTS**

I would like to express my gratitude to the almighty God for sustaining me throughout this undertaking. Furthermore, I am deeply thankful to my supervisor, Professor Brian Van Wyk, for his unwavering support during the course of my study. Your patience, knowledge, and guidance were second to none. Thank you so much, sir.

I would also like to extend my thanks to my mother. You always encouraged me when I felt discouraged and on the verge of giving up.

Additionally, I am grateful to my husband, Kaala, for his relentless support in making my dream come true. I must not forget to acknowledge my son, Kaala (Jnr), for his patience, even when I had to sacrifice my time with him to reach the finishing line. Thank you, Kaala.

Finally, I would like to express my appreciation to all those who played a role in my success, even if I haven't mentioned them by name. Thank you all.



#### ABSTRACT

Antiretroviral therapy (ART) has significantly enhanced the quality of life for individuals living with HIV on a global scale. In order to effectively manage HIV, optimal adherence to ART is of utmost importance, particularly with the enhanced accessibility to treatment. Inadequate adherence to ART has the potential to foster drug resistance, consequently leading to escalated costs for both individuals and national ART programmes, as patients necessitate a switch to more costly second- and third-line antiretroviral (ARV) regimens. The outbreak of the coronavirus disease-19 (COVID-19) and the subsequent implementation of national restrictions in Zambia disrupted the provision of HIV services, thereby exacerbating the challenge of adhering to ART for individuals living with HIV.

A quantitative, cross-sectional study was undertaken to ascertain the factors associated with adherence to ART among patients receiving care at a primary health care facility in Livingstone, Zambia. Data routinely collected from all patients on ART at this primary care health facility in Livingstone District, spanning from February 2020 to August 2022, were extracted from the electronic medical records. These data were then subjected to bivariate and multivariate regression analyses employing the Statistical Package for the Social Sciences (SPSS) version 28.

In this study, viral suppression was 92.9% (completely suppressed) and 7.1% (unsuppressed) respectively. The findings of the study indicate that being female (AOR = 1.41; 95% CI: 1.02– 1.96), having more than five years of experience with ART (AOR = 10.12; 95% CI: 5.41– 18.91), and having baseline and latest CD4 counts above 350 cells/mm<sup>3</sup> (AOR = 6.85; 95% CI: 3.84–12.20; AOR = 2.02; 95% CI: 1.18–3.47) were significant predictors of higher viral suppression. Conversely, the odds of viral suppression were significantly lower for the adult HIV population currently on the second-line regimen (AOR = 0.21; 95% CI: 0.12–0.38), those who were not switched to a more efficacious ARV regimen (AOR = 0.17; 95% CI: 0.11–0.26), those who were never initiated on TB prophylaxis (AOR = 0.36; 95% CI: 0.26–0.51), those who were not optimally adherent to ART in the last three days (AOR = 0.23; 95% CI: 0.15–0.36), and those who were not retained in care (AOR = 0.18; 95% CI: 0.13–0.25).

As of August 2022, the overall retention in care in this study was 87.1% (retained) and 12.9% (not retained) respectively as of August 2022. Regarding retention in care, the odds were higher for the adult HIV population with more than five years of experience with ART (AOR = 8.78;

95% CI: 4.94–15.62). Conversely, the odds of retention in care were lower for the adult HIV population who were not switched to a more efficacious regimen (AOR = 0.20; 95% CI: 0.14-0.29), those who were never initiated on TB prophylaxis (AOR = 0.31; 95% CI: 0.24-0.40), those who were not optimally adherent to ART in the last 3 days (AOR = 0.16; 95% CI: 0.12-0.23), and those who were not virally suppressed (AOR = 0.18; 95% CI: 0.13-0.25).

Tailored interventions are necessary to improve viral suppression rates especially for males, and address risk factors such as late presentation with HIV, poor adherence and retention in care. Further, health services factors should be addressed to improve quality of care to HIV patients, with particular emphasis on timely switching to more efficacious ART regimens.

**Keywords:** HIV, Adherence, retention in care, antiretroviral therapy, COVID-19, adults, viral suppression, AIDS, Zambia



# TABLE OF CONTENTS

DECLARA	TIONi
ACKNOWI	LEDGEMENTSii
ABSTRAC	Г ііі
LIST OF TA	ABLESviii
LIST OF FI	GURES viii
LIST OF A	BBREVIATIONS AND ACRONYMSix
CHAPTER	1: INTRODUCTION
1.1 BA	CKGROUND1
1.1.1	Magnitude of the HIV pandemic1
1.1.2	COVID-19 and HIV2
1.2 PR	OBLEM STATEMENT
1.3 AI	M AND OBJECTIVES
1.4 OU	JTLINE OF MINI-THESIS4
CHAPTER	2: LITERATURE REVIEW
2.1 IN	TRODUCTION
	EFINITION OF ADHERENCE TO ANTIRETROVIRAL THERAPY5
2.3 MI	EASUREMENT OF ADHERENCE
2.3.1	Self-reporting
2.3.2	Pharmacy refill data6
2.3.3	Clinic attendance (adherence to appointments)6
2.4 FA	CTORS ASSOCIATED WITH VIRAL SUPPRESSION, RETENTION IN
CARE, A	ND ADHERENCE TO ANTIRETROVIRAL THERAPY
2.4.1	Viral load suppression and adherence to ART7
2.4.2	Retention in care
2.5 BA	ARRIERS TO ADHERENCE

2.	5.1	Barriers to adherence	15
2.	5.2	Socio-demographic factors	16
2.	5.3	Health system factors	18
2.	5.4	Regimen characteristics	19
CHAP	TER 3	3: METHODOLOGY	21
3.1	INT	TRODUCTION	21
3.2	ST	UDY DESIGN	21
3.3	ST	UDY SETTING	21
3.4	ST	UDY POPULATION AND SAMPLING	22
3.5	DA	TA COLLECTION	23
3.6	DA	TA ANALYSIS	23
3.7	VA	LIDITY AND RELIABILITY	23
3.8	ET	HICS CONSIDERATIONS	24
CHAP	TER 4	4: RESULTS	25
4.1	INT	FRODUCTION	25
4.2	СН	ARACTERISTICS OF STUDY PARTICIPANTS	25
4.3	DE	TERMINANTS OF VIRAL SUPPRESSION	
4.	3.1	Socio-demographic factors	
4.	3.2	Clinical factors	
4.	3.3	Treatment factors	31
4.	3.4	Behavioural factors	32
4.4	DE	TERMINANTS OF RETENTION IN CARE	
4.	4.1	Socio-demographic factors	
4.	4.2	Clinical factors	
4.	4.3	Treatment factors	
4.	4.4	Behavioural factors	
CHAP	TER :	5: DISCUSSION	

5.1	INTRODUCTION			
5.2	PROFILE OF THE ADULT HIV POPULATION ON TREATMENT			
5.3	DETERMINANTS OF VIRAL SUPPRESSION43			
5.4	DETERMINANTS OF RETENTION IN CARE4			
5.5	SUMMARY			
СНАРТ	ER 6: CONCLUSIONS AND RECOMMENDATIONS			
6.1	INTRODUCTION47			
6.2	CONCLUSIONS			
6.3	LIMITATIONS OF THE STUDY			
6.4	RECOMMENDATIONS			
6.3	.1 Interventions to address identified risk factors			
6.3	.2 Exploring barriers to viral suppression and retention in care			
6.3	.3 COVID pandemic and preparedness			
REFERENCES				
APPENDIX 1: UWC ethics clearance letter				
APPENDIX 2: MUSOMHS ethics clearance letter				
APPENDIX 3: NHRA clearance letter				
APPENDIX 4: Permission letter from Livingstone DHO85				
APPENDIX 5: Confirmation of professional editing86				

# WESTERN CAPE

## LIST OF TABLES

## LIST OF FIGURES

010

1111

# WESTERN CAPE

# LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
COVID-19	Coronavirus disease 2019
HIV	Human immunodeficiency virus
МОН	Ministry of Health
PLWH	People Living With HIV
SSA	Sub-Saharan Africa
VL	Viral load
VMMC	Voluntary Medical Male Circumcision
WHO	World Health Organization

UNIVERSITY of the WESTERN CAPE

### **CHAPTER 1: INTRODUCTION**

#### **1.1 BACKGROUND**

The outbreak of SARS-CoV-2 (COVID-19) was declared a global health emergency by the World Health Organization (WHO) in March 2020 (Cucinotta & Vanelli, 2020). The COVID-19 pandemic has had a significant impact on public health, the economy, and social well-being worldwide (WHO, 2020). At the individual level, COVID-19 has had a profound effect on the physical and mental health of individuals, while at the community level, it has resulted in widespread disruption of social and economic systems (Chenneville *et al.*, 2020; WHO, 2020). Furthermore, COVID-19 has caused severe disruptions in health services due to the overwhelming number of cases, which strained health care systems, and the response measures implemented to address the pandemic, which impacted routine service delivery (Hogan *et al.*, 2020).

According to WHO (2020), the increased mortality affecting the AIDS response in sub-Saharan Africa due to COVID-19 can be attributed not only to the response measures but also to reduced quality of clinical care caused by strained health care facilities, regime change, and streamlined adherence counselling. In low- and middle-income countries such as Zambia, the primary concern is the impact of the pandemic on pre-established public health priorities, namely HIV, tuberculosis (TB), and malaria (Hogan *et al.*, 2020). When the first COVID-19 case was reported in Zambia on March 18, 2020, the Zambian government implemented mitigation measures, including the use of masks, school closures, restrictions on public gatherings, and limitations on access to hospitals and health centres, in order to curb the spread of the virus (Phiri *et al.*, 2022).

# 1.1.1 Magnitude of the HIV pandemic

Globally, approximately 38.4 million individuals were living with HIV (WHO, 2022). By the end of 2021, there were a total of 1.5 million new infections reported, with 28.2 million individuals accessing antiretroviral therapy (UNAIDS, 2020). Sub-Saharan Africa is home to two-thirds of the global population living with HIV (PLHIV). In 2021, the region accounted for a total of 25.6 million PLHIV (WHO, 2022). At the end of 2021, approximately 75% of people living with HIV globally were receiving antiretroviral therapy, a significant increase from 25% in 2010. Moreover, 81% of the 1.3 million pregnant women living with HIV at the

end of 2021 had access to antiretroviral therapy for maternal prevention of child transmission. The number of children aged 0-14 years living with HIV worldwide was 1.7 million at the end of 2021, compared to 2.5 million in 2010 (WHO, 2022).

#### 1.1.2 COVID-19 and HIV

The co-occurrence of COVID-19 and HIV poses a substantial public health challenge (Zikargae, 2020). PLHIV are affected by COVID-19 in various ways, including an increased susceptibility to contracting the virus, disruptions to HIV treatment and care, and interruptions in the supply chains for medication (Gatechompol *et al.*, 2021; Nagarakanti *et al.*, 2021). National measures implemented to contain the spread of the COVID-19 virus have disrupted access to facility-based health services such as medication pickups, adherence counselling, and support groups (Dyer *et al.*, 2021; Van Wyk & Mayman, 2022). These disruptions may lead to missed clinical appointments and pharmacy refills for PLHIV. Additionally, restricted access to health facilities designated as ART access points and limited personnel to prevent staff exposure to COVID-19 could impede adherence to antiretroviral therapy (Muchena & Kalenga, 2021).

Apart from the public health consequences, COVID-19 has had broader implications affecting PLHIV. The pandemic has exerted a significant impact on the informal economy, resulting in increased unemployment, reduced income generation, and widespread food insecurity (Nyoni & Okumu, 2020).

### **1.2 PROBLEM STATEMENT**

Significant progress has been achieved in the management of patients with HIV/AIDS since the introduction of antiretroviral drugs (ARVs). Non-compliance with prescribed medical protocols poses a multifaceted challenge, particularly for individuals with chronic conditions (Monjok, Smesny & Essien, 2009). People living with HIV (PLHIV) require daily doses of ARVs to control their illness and minimise the risk of transmission, but disruptions in care can impede their ability to adhere to the medication regimen (Iacob *et al.*, 2017). Non-adherence to treatment protocols diminishes the immunological benefits of antiretroviral therapy, making patients more susceptible to opportunistic infections, drug resistance, and HIV transmission (Wasti *et al.*, 2012). The emergence of the COVID-19 pandemic has caused substantial disruptions in health care delivery, including HIV treatment services (Hogan et al., 2020). Several recent studies have discussed or modelled the potential impact of the COVID-19 pandemic on HIV, while others have asked people living with HIV how they fared during the pandemic through surveys or qualitative interview results (Drain and Garrett, 2020; Jiang, Zhou and Tang, 2020). A quantitative study conducted at a high-level referral health facility in Lusaka, Zambia found that 9.0% of the 7,281 adult PLHIV included in the study had a detectable viral load, regardless of medication refill interval. This focused on adults with HIV infection who started treatment during the COVID-19 epidemic waves, as opposed to those who started treatment before the pandemic, suggesting this that the pandemic impacted ART adherence among adults living with HIV in Lusaka, Zambia (Kafwanka, Nalule and Michelo, 2023). However, the services provided by high-level referral health facilities differ significantly from the services provided in lower-level health facilities such as health centres, making it imperative to conduct a study at this level of health service delivery. Given the impact of the pandemic on healthcare and the restrictions on hospitals and health centres where ART patients receive their medications, it is critical to examine the factors that influence ART adherence among PLHIV accessing services at all levels of care including during the COVID-19 pandemic.

#### **1.3 AIM AND OBJECTIVES**

The aim of this study is to investigate the factors linked to adherence to antiretroviral therapy (ART) among patients attending a primary health care facility in Livingstone, Zambia, amid the COVID-19 pandemic.

The objectives of this study were:

- To describe the socio-demographic, clinical, treatment and behavioural characteristics of patients accessing ART services at a primary health care facility in Livingstone during the COVID-19 pandemic.
- To describe treatment outcomes (viral suppression and retention in care) of patients accessing ART services at a primary health care facility in Livingstone during the COVID-19 pandemic.
- To describe adherence among patients accessing ART services at a primary health care facility in Livingstone during the COVID-19 pandemic.
- To determine risk factors for ART adherence at a primary health care facility in Livingstone during the COVID-19 pandemic.

#### **1.4 OUTLINE OF MINI-THESIS**

presented.

*Chapter 2: Literature Review:* This chapter provides a comprehensive review of pertinent literature pertaining to various aspects of adherence in ART. The topics covered include the definition of adherence in ART, prevalence and measurement of adherence in sub-Saharan Africa, the relationship between viral load suppression and adherence to ART, the association between retention in care and adherence to ART, and the factors influencing ART adherence. *Chapter 3: Methodology:* This chapter delineates the methodology employed in the present study, encompassing the study design, sampling methods, and approaches utilised for data collection and analysis. It also elucidates the measures taken to enhance the reliability and validity of the study's findings. Additionally, a thorough account of ethical considerations is

*Chapter 4: Findings:* The findings of the study are expounded upon in this chapter. Descriptive and analytical analyses are employed to present the results in relation to the study's aims and objectives.

*Chapter 5: Discussion:* In this chapter, the study's findings are comprehensively discussed and contextualised. A comparison is drawn between the current study's findings and the relevant literature.

*Chapter 6: Conclusions and Recommendations:* This chapter offers conclusions and recommendations derived from the research findings, taking into account the limitations of the study.

UNIVERSITY of the WESTERN CAPE

### **CHAPTER 2: LITERATURE REVIEW**

#### 2.1 INTRODUCTION

The previous chapter provided a background and introduction to the study. This chapter focuses on a review of literature. The literature review addresses the following areas: the definition of adherence in ART, the prevalence and measurement of adherence in sub-Saharan Africa, and the measurement of adherence as well as the factors influencing ART adherence.

### 2.2 DEFINITION OF ADHERENCE TO ANTIRETROVIRAL THERAPY

Medication adherence has been defined as the degree to which a patient follows the prescribed medication regimen provided by a health care professional (Urquhart, 1996). To attain and maintain viral suppression in individuals receiving ART, it is essential to adhere optimally, which entails taking more than 90% of the prescribed medication as directed by the health care professional (Altice *et al.*, 2019). Adherence to ART plays a crucial role in determining the outcomes of HIV treatment, as satisfactory adherence is associated with viral suppression and consequently improved clinical results (Nachega *et al.*, 2012; Paterson *et al.*, 2000).

#### 2.3 MEASUREMENT OF ADHERENCE

Measuring adherence assists in determining the likelihood of treatment success or failure for a patient. Adherence can be assessed either directly or indirectly. Direct measures encompass therapeutic drug monitoring or direct observation of treatment consumption. Indirect measures comprise self-reporting (Glass & Cavassini, 2014; Marcellin *et al.*, 2013), pill counts (Arnsten *et al.*, 2002; Liu *et al.*, 2001), pharmacy dispensing data (Bisson *et al.*, 2008; Steiner & Prochazka, 1997), clinic attendance for medication refill (Kunutsor *et al.*, 2010), and viral load monitoring (Ross-Degnan *et al.*, 2010; Stricker *et al.*, 2014; Tanyi *et al.*, 2021).

Associations have been observed between socio-demographic, clinical, treatment, and behavioural characteristics of people living with HIV (PLHIV) and viral suppression, as well as retention in care. These associations can be employed to gauge adherence to ART (Haider *et al.*, 2021; Sok *et al.*, 2021). Monitoring viral load is a vital and cost-effective strategy for PLHIV, enabling the identification of poor adherence to ART and the detection of treatment failure, owing to its commendable specificity and sensitivity (Barnabas *et al.*, 2017; Glass, Myer & Lesosky, 2020).

However, it is important to note that while viral load suppression serves as an encouraging indication of acceptable adherence to ART, an unsuppressed viral load does not always unequivocally signify poor adherence (Flynn *et al.*, 2004; Murphy *et al.*, 2001; Wiener *et al.*, 2004).

#### 2.3.1 Self-reporting

Adherence measurement can involve health care professionals inquiring about the frequency of missed tablets over multiple days and documenting the responses (Simoni *et al.*, 2006). However, the accuracy of self-reporting as a method for measuring adherence has been questioned, as it has been found to overestimate adherence (Glass & Cavassini, 2014; Marcellin *et al.*, 2014). Moreover, self-reports are susceptible to recall bias. To assess adherence, three indicators have been proposed: the percentage of compliance for each patient, the percentage of patients fully adhering to ART, and the percentage of antiretroviral (ARV) doses taken by patients during the recall period (last three days) (Ross-Degnan *et al.*, 2010).

#### 2.3.2 Pharmacy refill data

This adherence measure relies on monitoring the number of pills dispensed to a patient within a specific time frame and tracking their return to the pharmacy for refills. For instance, if a patient fails to refill a 60-day prescription for 65 days, it suggests that they may have missed taking the medication for five of those days (Grimes *et al.*, 2013).

#### **2.3.3** Clinic attendance (adherence to appointments)

Regular clinic visits, encompassing drug pickups, routine clinical examinations, and laboratory tests, are emphasised by Abdulrahman *et al.* (2019) as vital for treatment success. Non-adherence can be indicated by missed scheduled appointments, highlighting the importance of clinic attendance as a measure of adherence (Ross-Degnan *et al.*, 2010).

# 2.4 FACTORS ASSOCIATED WITH VIRAL SUPPRESSION, RETENTION IN CARE, AND ADHERENCE TO ANTIRETROVIRAL THERAPY

This section discusses factors that are associated with viral suppression, retention in care, and adherence to antiretroviral therapy.

#### 2.4.1 Viral load suppression and adherence to ART

Suboptimal adherence to ART among people living with HIV (PLHIV) results in the lack of viral control and adverse clinical outcomes, including virologic failure (Howard *et al.*, 2002; Nachega *et al.*, 2007), accelerated disease progression (Bangsberg *et al.*, 2001; Detels *et al.*, 1998), the emergence of drug-resistant viruses (Bangsberg *et al.*, 2000; Bangsberg, Moss & Deeks, 2004; Wainberg & Friedland, 1998), and an increased risk of secondary HIV transmission (Cohen *et al.*, 2011; Loutfy *et al.*, 2013).

According to the WHO (2020) consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, treatment success is defined by a viral load threshold of < 1000 copies/mL, with individuals achieving this threshold considered virally suppressed. PLHIV with a viral load > 1000 copies per millilitre are deemed *virally unsuppressed* and are advised to undergo enhanced adherence counselling (EAC). Subsequently, a repeat viral load test is conducted three months later to determine viral suppression or unsuppression (Bvochora *et al.*, 2019; Kaira *et al.*, 2021; MOH, 2020).

#### 2.4.1.1 Socio-demographic characteristics associated with viral suppression

Existing literature highlights the significance of socio-demographic characteristics, including age, gender, and marital status, in relation to viral suppression among people living with HIV (PLHIV) (Okonji *et al.*, 2021; Ntombela *et al.*, 2022).

### Age

The relationship between age and viral suppression in PLHIV has been examined in several studies, yielding varied findings. A cross-sectional analysis involving 17,044 HIV-infected adults across 14 clinical cohorts in the U.S. and Canada identified age as a predictor of viral suppression (Yehia *et al.*, 2015). Similarly, a multicentre study conducted in South Africa found that older age was significantly associated with higher rates of virological suppression among HIV-infected patients receiving ART (Fatti *et al.*, 2014). Consistent with these findings, a study in Kenya reported that older age was significantly associated with higher rates of viral suppression among HIV-infected adults (Nyaboke *et al.*, 2023). Moreover, a study conducted in South Africa found that older age was linked to higher rates of adherence to ART and better viral suppression among HIV-infected patients (Peltzer *et al.*, 2010). However, a study by Lokpo *et al.* (2020) found no statistically significant relationship between age and viral suppression.

#### Gender

Studies conducted in various African countries have yielded mixed results regarding the association between gender and viral suppression. Studies in Uganda (Wakooko, Gavamukulya & Wandabwa, 2020) and Nigeria (Isaac *et al.*, 2021) found no significant association between gender and viral suppression among HIV-infected adults. Conversely, studies conducted in South Africa (Azia, Mukumbang & Van Wyk, 2016) and Ethiopia (Desta *et al.*, 2020) indicated that males were more likely to achieve viral suppression than females among PLHIV. However, a study conducted in Zambia found similar rates of viral suppression between males and females aged 15–24 years (Avert, 2016).

#### Marital status

An increasing body of research has explored the relationship between marital status and viral suppression among PLHIV. Various studies have identified marital status as a significant predictor of HIV treatment outcomes, including viral suppression. A systematic review and meta-analysis conducted in sub-Saharan Africa (Green *et al.*, 2020) and a study in South Africa (Ntombela *et al.*, 2022) both found that being married or cohabiting was associated with higher rates of viral suppression among HIV-positive adults in care. In South Africa, being single was associated with lower rates of viral suppression among HIV-positive adults receiving ART (Mogosetsi *et al.*, 2018). However, other studies have reported a weaker association between marital status and viral suppression. A study conducted in Ghana found no significant association between marital status and viral suppression (Lokpo *et al.*, 2020).

# 2.4.1.2 Clinical characteristics associated with viral suppression

Existing literature highlights several clinical factors that are of high importance in achieving viral suppression among people living with HIV (PLHIV). These factors include the duration on ART, baseline CD4 counts, the WHO clinical stage at ART initiation, and the presence of opportunistic infections and a history of tuberculosis (Ayele *et al.*, 2015; Bulage *et al.*, 2017; Lokpo *et al.*, 2020).

#### Duration on ART

Studies conducted in various African countries, such as South Africa (Berihun *et al.*, 2023; Haghighat *et al.*, 2021), Kenya (Cherutich *et al.*, 2016), and Ghana (Lokpo *et al.*, 2020), have

consistently reported that longer durations on ART are associated with a higher likelihood of viral suppression in PLHIV.

#### CD4 count

In the majority of countries in sub-Saharan Africa, including Southern Africa, the universal test-and-treat strategy has been adopted (WHO, 2017). Studies have shown an association between immunosuppression and viral suppression among children and adults on ART. Unsuppressed viral loads are more commonly observed in patients with WHO clinical stage III and IV, those under the age of 20, and individuals with CD4 counts below 350 cells/mm<sup>3</sup> (Bennett *et al.*, 2002; Bonnet *et al.*, 2005; Grabar *et al.*, 2005; Jobanputra *et al.*, 2015). Additionally, studies conducted in Tanzania (Muri *et al.*, 2017) and Nigeria (Abdullahi *et al.*, 2021) have suggested that higher CD4 counts at ART initiation are associated with better viral suppression.

#### WHO clinical stage

International studies have demonstrated the effectiveness and precision of the WHO Clinical Staging system in managing HIV-infected patients. There is agreement between the clinical manifestations listed in the WHO staging system and laboratory markers such as CD4 cell count and total lymphocyte count (Weinberg & Kovarik, 2010). The WHO staging system categorises patients into one of four hierarchical clinical stages, ranging from stage I (asymptomatic) to stage IV (AIDS). Patients are placed in a stage when they exhibit at least one clinical condition listed in the stage's criteria. Even if the underlying clinical condition that initially placed individuals in that stage is resolved, they remain in the higher stage (Malamba et al., 1999). Studies conducted in various African countries have investigated the association between WHO staging and viral suppression (Jobanputra et al., 2015). For instance, a study conducted in Swaziland reported that individuals with WHO stage III and IV disease and CD4 counts < 350 cells/mm<sup>3</sup> were more likely to be virally unsuppressed. In a prospective study conducted in South Africa, which followed up with adolescents for two years, it was found that individuals who were WHO stage IV at baseline had better viral suppression at months 12 and 24, while those with WHO stage III at baseline had better viral suppression at month 4 (Kriel, 2017).

#### HIV-TB co-infection

Among individuals living with HIV, tuberculosis (TB) remains a significant cause of morbidity and mortality. African nations bear a disproportionate burden of HIV-associated TB, particularly among the most vulnerable populations who are at risk for both TB and HIV (Hamada *et al.*, 2021; Dye *et al.*, 2006; Karim *et al.*, 2009). According to the 2018 Global TB report, sub-Saharan Africa faces a high burden of TB, primarily due to the increased prevalence of TB-HIV co-infection, with over 51% of TB cases being co-infected with HIV (WHO, 2018b). A study conducted in Uganda identified active TB as a factor associated with reduced viral suppression among individuals living with HIV (Bulage *et al.*, 2017). Similarly, a study in South Africa focusing on factors associated with unsuppressed viral load among adolescents receiving first-line ART for more than six months reported that individuals on TB treatment were less likely to achieve viral suppression (Joseph Davey *et al.*, 2018).

#### 2.4.1.3 Treatment characteristics associated with viral suppression

Treatment characteristics, including the current antiretroviral (ARV) regimen and changes to an efficacious ART regimen, have been identified as important factors in achieving viral suppression (Barry *et al.*, 2013; Esber *et al.*, 2022; Nabitaka *et al.*, 2020).

#### Current ARV Regimen/Change in ART regimen and viral suppression

Epidemiological studies have demonstrated that patients on first-line ART exhibit high rates of viral suppression, indicating that streamlined care could potentially eliminate HIV (Barry *et al.*, 2013). Furthermore, studies have shown that transitioning people living with HIV (PLHIV) to a more efficacious regimen, such as a dolutegravir-based regimen, improves or maintains viral suppression. A retrospective study conducted in Ethiopia on virological suppression and its associated factors of a dolutegravir (DTG)-based regimen found that viral suppression among PLHIV increased post-DTG initiation (92%) compared to pre-DTG initiation (81.4%) (Mehari *et al.*, 2021). Similar findings have been reported in Uganda (Nabitaka *et al.*, 2020) as well as in Kenya, Nigeria, and Tanzania (Esber *et al.*, 2022).

#### 2.4.1.4 Behavioural characteristics associated with viral suppression

Behavioural characteristics, such as optimal adherence and retention in care, have been identified as critical factors in achieving viral suppression (Umeokonkwo *et al.*, 2019).

#### Optimal adherence in the last three days

Optimal adherence to ART among PLHIV is crucial for attaining and sustaining virological suppression (Byrd *et al.*, 2019; Umeokonkwo *et al.*, 2019). A study conducted in Rwanda aimed to investigate high levels of adherence and viral suppression in a nationally representative sample of HIV-infected adults on ART for 6, 12, and 18 months. The study found that all participants who were optimally adherent demonstrated higher rates of viral suppression compared to those who were not optimally adherent (Elul *et al.*, 2013). Similarly, a study conducted in Kenya indicated that optimal adherence to ART increased the likelihood of viral suppression (Nyaboke *et al.*, 2023).

#### Retention in care

Studies conducted within and outside Africa have revealed an association between viral suppression and retention in care. Studies conducted in the United States by Giordano *et al.* (2007) and in South Carolina by Tripathi *et al.* (2011) demonstrated this association. Moreover, studies conducted in Zimbabwe (Mutasa-Apollo *et al.*, 2014) and Nigeria (Onoka *et al.*, 2013) found a positive correlation between retention in care and viral suppression. According to Umeokonkwo *et al.* (2019), retention in care serves as an indicator of high-quality care and is crucial for patients to achieve viral suppression and other positive outcomes from HIV treatment.

#### 2.4.2 Retention in care

Retention in care refers to the state of being alive and receiving ART without being transferred to other health care facilities for ongoing treatment (Massaquoi *et al.*, 2009; Rosen *et al.*, 2007). Sustaining retention in care enables HIV-infected patients on ART to receive continuous treatment, leading to improved clinical outcomes (Geng *et al.*, 2010a). Suboptimal retention in care results in non-adherence to ART, increasing the risks of HIV transmission, drug-resistant mutations, morbidity, and mortality (Clouse *et al.*, 2013). Adherence to treatment and retention in care are crucial for achieving viral suppression (Gardner *et al.*, 2011; Park *et al.*, 2007; Viswanathan *et al.*, 2015). The current Consolidated Guidelines for HIV Management in Zambia classify people living with HIV (PLHIV) as 'lost to follow-up' (LTFU) if they are 30 days past their scheduled refill date (MOH, 2020).

#### 2.4.2.1 Socio-demographic characteristics associated with retention in care

Age, gender, and marital status have been identified as important factors in achieving retention in care among PLHIV on ART (Nicol *et al.*, 2022; Umeokonkwo *et al.*, 2019).

#### Age

Studies have reported varied findings regarding the association between age and retention in care. After initiating ART, a low proportion of PLHIV under 25 years old are successfully retained in care. Factors such as stigma and discrimination, distance and transportation barriers, poverty and unemployment, work and child care responsibilities, and social relationships have been identified as major determinants of poor retention in HIV care (Eduardo *et al.*, 2014; Geng *et al.*, 2010b; Lamb *et al.*, 2014; Zanoni & Mayer, 2014). A study conducted in mid-western Uganda found that 70% of adolescents were not retained in care, with older adolescents (15–19 years) having lower retention rates compared to younger adolescents (10–14 years) due to ART duration and age-related factors (Geng *et al.*, 2010; Izudi *et al.*, 2018). Another study focusing on older adults in western Kenya observed that individuals aged 50 years and above, who initiated treatment, demonstrated better retention in care compared to younger adults below 50 years old (Kiplagat *et al.*, 2018).

#### Gender

A study on linkage to HIV Care and Early Retention in Care Rates in the Universal Test-and-Treat Era in KwaZulu-Natal indicated that gender and age played a significant role in HIV testing and retention in care. The study reported a significantly higher proportion of females testing for HIV and being retained in care at 12 months compared to males (Nicol *et al.*, 2022). Similar findings were reported in a study conducted in South Africa (Hirasen *et al.*, 2020) and another study in sub-Saharan Africa (Staveteig *et al.*, 2013).

#### Marital status

Marital status has been the focus of several studies examining its association with retention in HIV care. A study conducted in Nigeria identified marital status as a statistically significant predictor of retention among individuals accessing care in private health facilities (Umeokonkwo *et al.*, 2019). The study found that married participants were more likely to be retained in care compared to those who were unmarried. Similarly, a study conducted in rural southwestern Uganda on retention in HIV care among youths aged 15-24 years found that being married was significantly associated with higher retention rates. Marriage or having a spouse

provides psychological and emotional support, which promotes retention in HIV care (Muwanguzi *et al.*, 2021; Santos *et al.*, 2018). A systematic review and meta-analysis conducted in Ethiopia on HIV patient retention and attrition in care identified being unmarried as a major determinant of attrition (Abebe Moges *et al.*, 2020).

#### 2.4.2.2 Clinical characteristics associated with retention in care

Several clinical characteristics, including WHO clinical stage, CD4 count, duration on treatment, and HIV-TB co-infection, play a crucial role in ensuring the retention in care of people living with HIV (PLHIV) on ART (Kiwanuka *et al.*, 2020; Shah *et al.*, 2022; Tsague *et al.*, 2008).

#### WHO clinical stage

The association between WHO clinical stage and retention in care has been examined by various researchers. A study conducted in the Democratic Republic of the Congo (DRC) found that patients at WHO clinical stage I had significantly higher odds of being retained in care compared to those at stage IV (Shah *et al.*, 2022). Similarly, a study conducted in Uganda reported that patients who initiated ART with HIV disease classified as WHO stage III or IV had a 35% higher risk of being lost to follow-up (LTFU) compared to those with WHO stage I or II (Kiwanuka *et al.*, 2020).

#### CD4 count

In Uganda, a study found that patients who initiated ART with a baseline CD4 cell count of 200–350 cells/mm<sup>3</sup> had a 21% higher risk of being LTFU compared to those with a baseline CD4 cell count of 200 cells/mm<sup>3</sup> (Kiwanuka *et al.*, 2020). Conversely, a study conducted in Cameroon reported that having a CD4 count greater than 200 cells/mm<sup>3</sup> at the start of treatment was associated with higher retention compared to having a CD4 count less than 200 cells/mm<sup>3</sup> (Rogers *et al.*, 2021).

#### Duration on treatment

A systematic review conducted in sub-Saharan Africa from 2007 to 2009 found that the longer patients were on ART, the higher the likelihood of retention in care (Fox & Rosen, 2010). However, a study in the DRC, focusing on factors associated with the retention of HIV patients on ART, found an inverse association between the length of time on ART and the likelihood

of retention. Patients on ART for 7 months had more than 7 times higher odds of retention compared to those on ART for 53 months or longer (Shah *et al.*, 2022).

#### HIV-TB co-infection

TB is a well-known risk factor for poor outcomes and non-retention in HIV clinics in sub-Saharan Africa and other developing countries (Gunda *et al.*, 2016; Jalal *et al.*, 2017; Tsague *et al.*, 2008). A study conducted in Cameroon, where TB was diagnosed in 9% of patients at enrolment, found that patients with active TB at enrolment were more likely to drop out of the programme within the first six months of starting ART compared to those without TB (Tsague *et al.*, 2008).

#### 2.4.2.3 Treatment characteristics associated with retention in care

Treatment characteristics have been identified as important factors in ensuring the retention in care of people living with HIV (PLHIV) on ART (Bor *et al.*, 2022).

#### Current ARV regimen/Change in ART regimen

The use of simplified drug regimens has shown potential to improve the retention in care of chronic disease patients, including PLHIV (Bor *et al.*, 2022). In Zambia, for example, the adoption of a once-daily single-pill HIV treatment regimen as the standard of care in 2013, replacing a multiple-pill regimen, aimed to enhance treatment adherence and retention in care (MOH, 2014).

#### 2.4.2.4 Behavioural characteristics associated with retention in care

Optimal adherence to treatment is among the behavioural characteristics that have been identified as crucial for achieving retention in care (Stricker *et al.*, 2014).

#### Optimal adherence in the last three days

It is important to distinguish between retention in care and adherence to treatment. While retention in care refers to attending clinic appointments, adherence to treatment specifically refers to the proper intake of medication as prescribed. It has been suggested that the best outcomes are achieved when PLHIV are not only retained in care for clinical monitoring but also adhere to their treatment regimen (Stricker *et al.*, 2014). PLHIV who are not retained in care face challenges in accessing medications regularly, highlighting the critical role of retention in care in promoting medication adherence (Stricker *et al.*, 2014). Suboptimal

retention in HIV care has been associated with poor ART adherence and suboptimal virologic suppression, leading to worsened health outcomes (Frieden *et al.*, 2019; Kakkar *et al.*, 2016).

#### 2.5 BARRIERS TO ADHERENCE

Adherence to ART is influenced by various barriers and factors, including patient-related factors, socio-demographic factors, health care system factors, and clinical, treatment, and behavioural characteristics (Berhanu Billoro *et al.*, 2018; Carvalho *et al.*, 2019; Joseph *et al.*, 2015; Lee *et al.*, 2019).

#### 2.5.1 Barriers to adherence

This sub-section discusses some of the barriers to adherence.

#### 2.5.1.1 Patient-related factors

Patient-related barriers to adherence include non-disclosure of HIV status, alcohol use, lack of social support, forgetfulness, and myths related to antiretroviral (ARV) drugs (Azia *et al.*, 2016; Sahay *et al.*, 2011; Wasti *et al.*, 2012).

#### 2.5.1.2 Non-disclosure of HIV status

A study by Dessie *et al.* (2019) found that patients who disclosed their HIV serostatus had better social support, stronger family and relationship ties, and were consequently better able to adhere to ART and improve their adherence compared to those who did not disclose their HIV status.

# 2.5.1.3 Alcohol use

Research has shown that individuals taking ART and consuming alcohol are more likely to experience missed doses, medication lapses, and treatment failure, which can be attributed to alcohol-induced cognitive impairment (Braithwaite *et al.*, 2007; Hendershot *et al.*, 2009). Furthermore, at least 25% of ART patients discontinue their medication when drinking alcohol (Kalichman *et al.*, 2009; Sankar, Rameh & Sunny, 2018).

#### 2.5.1.4 Lack of social support

Martos-Méndez (2015) highlights that social support enhances adherence self-efficacy, enabling people living with HIV to overcome adherence barriers. Adherence to medication for specific diseases is associated with having friends or providers who consistently support

patients in meeting their needs (Scheurer *et al.*, 2012). A study conducted in Thailand reported that social support from family members facilitated ART adherence, while feelings of being unloved or neglected and relationship turmoil were identified as barriers to adherence (Knodel *et al.*, 2010).

#### 2.5.1.5 Forgetfulness

Forgetfulness, the inability to recall information, can lead to disruptions in daily activities such as taking prescribed ART doses, resulting in non-adherence among people living with HIV (Barfod *et al.*, 2006; Chesney *et al.*, 2000; Harzke *et al.*, 2004; Joseph Afe, Motunrayo & Ogungbade, 2018; Nduaguba *et al.*, 2017; Okuku & Dan-Jumbo, 2021; Sauceda *et al.*, 2018; Spies *et al.*, 2019).

#### 2.5.2 Socio-demographic factors

Numerous studies conducted worldwide have identified associations between sociodemographic factors such as age, marital status, gender, employment status, and level of education and adherence to ART.

#### 2.5.2.1 Age

Studies by Nozaki *et al.* (2011) and Dorcélus *et al.* (2021) have reported better adherence among older patients (> 35 years) compared to those under 35 years of age. Possible contributing factors to this finding include financial dependence of younger HIV individuals on others, while non-adherence was associated with financial stability among older individuals (Ghidei *et al.*, 2013). Additionally, lower adherence in younger HIV patients has been attributed to social and psychological factors, inconsistent daily routines, fear of disclosure, forgetfulness, medication side effects, and a lack of understanding of the importance of medication even when feeling well (Dowshen *et al.*, 2011).

#### 2.5.2.2 Marital status

Married individuals are more likely to adhere to ART compared to unmarried individuals due to the support they receive from their partners (Graham *et al.*, 2013; Ngarina *et al.*, 2013; Sanjobo, Frich & Fretheim, 2008; Weiser *et al.*, 2010). Consistent with these findings, studies by Hiregoudar *et al.* (2019) and Wardhani and Yona (2021) have also found that married participants demonstrate higher adherence to ART compared to those with other marital statuses, primarily because of partner support. However, contradictory findings have been

reported in other studies, with one study suggesting that being widowed is associated with higher adherence to ART compared to other marital statuses (Filimão *et al.*, 2019), while another study found that marital status does not significantly affect ART adherence (Shigdel *et al.*, 2014).

#### 2.5.2.3 Gender

Inconsistencies persist regarding the association between gender and non-adherence, possibly due to confounding factors related to unexamined social or behavioural factors (De *et al.*, 2013). For instance, Cornell *et al.* (2012) found that men were more likely than women to discontinue ART, although no clear explanation for this gender difference was provided. Similarly, a study evaluating the uptake of ARVs reported that men who tested positive were less likely to seek treatment due to fears of marital discord, as it was assumed that men who tested positive had acquired HIV through infidelity (Campbell *et al.*, 2011; Muula & Kataika, 2008; Skovdal *et al.*, 2011). However, contradicting the aforementioned findings, Marcellin *et al.* (2014) and Graham *et al.* (2013) reported that men demonstrate higher adherence to ART compared to women.

#### 2.5.2.4 Employment status

Differences in adherence based on employment status have been linked to gender roles and employment inequalities (Nachega *et al.*, 2015). The direct effects of workload, such as physical and mental fatigue and work schedules, can impact patient adherence (Adler & Newman, 2017). A meta-analysis revealed that employed HIV-infected patients from low-, middle-, and high-income countries were 39% more likely to adhere to ART compared to unemployed patients (Amekudzi *et al.*, 2014). Similarly, Rosa *et al.* (2015) reported that employed individuals showed higher adherence to ART than non-employed individuals. However, contradicting these findings, a recent study by Dorcélus *et al.* (2021) found no difference in adherence based on employment status.

#### 2.5.2.5 Level of education

Various studies have reported mixed results regarding the association between educational attainment and ART adherence. In an environment with a literacy rate of only 61% for adults over 15 years, Dorcélus *et al.* (2021) found no clear association between education and adherence. Conversely, Peltzer and Pengpid (2013) reported a positive association between education between education level and adherence. Similarly, a study conducted in Botswana demonstrated that

increasing a person's knowledge about ART through education improved adherence (Weiser et al., 2003).

#### 2.5.2.6 Financial status

A systematic review of 18 studies by Wasti et al. (2012) indicated that poor adherence was largely attributed to the financial burden associated with ART, including travel and diagnostic costs, which further complicated access. Transportation costs, health care facility expenses, and financial insecurity have also been identified as factors influencing adherence to ART (Bezabhe et al., 2014; Penn, Watermeyer & Evans, 2011; Skovdal et al., 2011).

#### 2.5.3 Health system factors

Health system factors can significantly influence adherence to ART among people living with HIV. These factors include long distance to health facilities, long waiting times, intermittent supply and stockouts of ARVs, and dissatisfaction with the care received.

#### 2.5.3.1 Long distance to health facilities

The accessibility of HIV care and treatment can impact adherence, although the association between longer travel distances and treatment outcomes is not consistently supported by evidence (Lankowski et al., 2014). Studies by Mannheimer et al. (2005, 2010) and Mocroft et al. (1999) suggest that travelling long distances to receive ART can hinder adherence. Another study on population uptake of antiretroviral treatment found that greater distance from the nearest clinic offering HIV treatment was negatively associated with ART uptake (Cooke et al., 2010). UNIVERSITY of the

2.5.3.2 Long waiting timesLong waiting times significantly affect patient satisfaction and health care service delivery, efficiency, quality, transparency, and accountability (Atnafu et al., 2015). Among the various factors that can have adverse effects on ART treatment outcomes, long waiting times have been reported (Mahomed & Bachmann, 1998). Factors such as shortages of medical staff, medical and laboratory supplies, and poor appointment systems contribute to prolonged waiting times (Mahomed & Bachmann, 1998).

#### 2.5.3.3 Dissatisfaction with care received

The provision of quality and comprehensive care is crucial for maintaining high levels of adherence and long-term viral suppression among people living with HIV (Mwangi *et al.*, 2008). Patient satisfaction and perceived quality of care, including health care personnel proficiency, health care delivery, resource availability, service accessibility, and cost of care, are important for the overall well-being of individuals living with HIV (Dansereau *et al.*, 2015; Devnani *et al.*, 2012). Patients' perceived satisfaction with HIV care, influenced by health care workers' skills, attitudes, and trustworthiness, can impact adherence to ART and indirectly affect viral suppression (Somi *et al.*, 2021).

#### 2.5.4 Regimen characteristics

Regimen characteristics, such as pill burden and side effects, have been identified as important factors influencing adherence to ART (Mbuagbaw *et al.*, 2012).

#### 2.5.4.1 Pill burden

Simplifying ART regimens is considered crucial for improving adherence (Nachega *et al.*, 2011). The number of pills that people living with HIV (PLHIV) need to take can influence their adherence to ART (Chesney *et al.*, 2000; Kalichman *et al.*, 2009). Several studies have examined the impact of simplified once-daily therapies compared to more complex regimens requiring twice-daily or more frequent dosing (Nachega *et al.*, 2011). A meta-analysis of 11 randomised controlled trials found that patients on once-daily dosing regimens had better adherence compared to those on twice-daily regimens (Parienti *et al.*, 2009). Similarly, multiple observational studies have shown that adherence is significantly better for individuals taking a single-dose regimen compared to those on multiple-dose regimens (Bangsberg *et al.*, 2010; Cohen, Meyers & Davis, 2013; Hanna *et al.*, 2014; Rao *et al.*, 2013). However, some studies have reported no association between pill burden and adherence to ART (Buscher *et al.*, 2012).

#### 2.5.4.2 Side effects

ART-related side effects are recognised as significant barriers to adherence (Ammassari *et al.*, 2001; Rao *et al.*, 2007). Overcoming and managing these side effects is crucial not only for maintaining high adherence but also for preserving a high quality of life (Zhang *et al.*, 2016). A study by Rao *et al.* (2007) found that many participants experienced side effects, leading

some to discontinue their medication. Interventions aimed at managing side effects have shown positive effects on ART adherence (Johnson *et al.*, 2011).



http://etd.uwc.ac.za

### **CHAPTER 3: METHODOLOGY**

#### 3.1 INTRODUCTION

The preceding chapter reviewed literature relevant to this study. This chapter discusses the research methodology used in the study.

#### **3.2 STUDY DESIGN**

The study design pertains to the systematic approach undertaken by researchers to address a specific research question. The selection of a study design fundamentally determines the manner in which data and measurements are collected and subsequently analyzed (Ehrlich & Joubert, 2014). In this study, a retrospective cross-sectional study design with a quantitative orientation was employed. This particular design facilitated an examination of the association between adherence and other variables of interest within the population accessing ART services at the Mahatma Gandhi Clinic during the COVID-19 pandemic. Given the focus and objectives of the study, this design was deemed most appropriate as it enabled the acquisition of information pertaining to past and present occurrences (Wang & Cheng, 2020). Furthermore, the design facilitated the concurrent measurement of multiple exposures, aligning well with the study's aims and objectives that investigated several exposures (Robson & McCartan, 2016).

### 3.3 STUDY SETTING

The study was conducted in Livingstone, the principal tourist hub of Zambia, located in the southern region of the country and situated approximately 485 km away from the capital city, Lusaka. According to the most recent census conducted by the Zambia Statistical Agency-ZSA (2022), the city has an estimated population of 177,393 individuals, with an HIV prevalence rate of approximately 25.3% (Gage, 2014).

The Mahatma Gandhi Clinic serves as a primary health care (PHC) facility and attends to the largest number of patients (2,350 as of 2021) receiving ART services. It is one of the two zonal health facilities in Livingstone and caters to a catchment area encompassing 29,920 people. Operating 24 hours a day, seven days a week, the facility offers a range of services, including outpatient care, ART/prevention of mother-to-child transmission (PMTCT), HIV testing services, family planning, laboratory and pharmacy services, mother and child health (MCH) services, cervical cancer screening, voluntary male medical circumcision, tuberculosis care, community health, and screening and vaccination services for SARS-CoV-2 (COVID-19). All

these services are provided free of charge with the support of the Ministry of Health (MOH). The clinic's personnel consists of 22 nurses (11 midwives and 11 general nurses), seven clinicians, one environmental health technologist, four laboratory technologists, two pharmacy technologists, one physician, one nutritionist, five hygiene assistants, six psychosocial counsellors, two data clerks, one community liaison officer, one registrar, two revenue collectors, and two guards (MOH).

#### 3.4 STUDY POPULATION AND SAMPLING

The concept of study population refers to a collective of individuals who possess one or more characteristics that are of interest to the researcher (Sekaran & Bougie, 2010). In this study, the research population comprised HIV-positive patients receiving ART at the Mahatma Gandhi Clinic in the Livingstone district, provided they met the specified eligibility criteria.

Inclusion criteria encompass the essential characteristics of the target population that researchers employ to address their research question, whereas exclusion criteria pertain to the additional attributes possessed by potential study participants who satisfy the inclusion criteria but may potentially influence the study's success or heighten the likelihood of adverse outcomes.

#### Inclusion criteria

The inclusion criteria for the eligible study population were as follows:

- HIV-positive patients aged > 18 years
- Receiving ART for a duration exceeding six months within the specified review period
- Accessing ART services at the Mahatma Gandhi Clinic in the Livingstone District

#### Exclusion criteria

The exclusion criteria for the ineligible study population were as follows:

- Patients who were enrolled in another concurrent study
- Patients intending to transfer out of the facility where the study was to be conducted during the designated study period

Sampling represents the process through which researchers select a sample of individuals to serve as research participants (Martinez-Mesa *et al.*, 2016). In this study, an all-inclusive sampling method was employed, involving the participation of all ART patients who met the inclusion criteria.

#### 3.5 DATA COLLECTION

To facilitate data extraction from the electronic medical record (EMR), the principal investigator enlisted the assistance of a research assistant. The data extraction was performed using a script developed with Structured Query Language (SQL). The designated period for data extraction spanned from March 2020 to August 2022. The EMR captures pertinent patient information, including medical history, prescribed medications, laboratory test results, vital signs, and personal details such as age, height, and weight. Health care providers rely on EMRs for diagnosis and day-to-day patient management, obviating the need to retrieve a patient's previous paper medical records and ensuring the accuracy and legibility of data. The extracted EMR dataset underwent screening, with only those individuals meeting the aforementioned eligibility criteria being included in the study. To extract the variables of interest, the research assistant executed a query on the EMR, exporting the query output to Excel subsequent to downloading.

#### **3.6 DATA ANALYSIS**

The downloaded data from the EMR, which was subsequently exported to Excel, underwent a review to identify missing values. Variables with completely missing values were automatically eliminated, and the analysis was conducted on the remaining cases with complete data records. The Statistical Software for the Social Sciences (SPSS v28) was employed for data analysis. A frequency table was generated to describe the socio-demographic, clinical, behavioural, and treatment characteristics of the study population. Bivariate analysis was employed to assess the strength of the association between the independent variables and the outcome variables, namely retention in care and viral suppression. Chi-square tests and crude odds ratios were used to examine and quantify the associations. Variables that exhibited significant associations with retention in care and viral suppression during the bivariate analysis, at a significance level of 5%, were included in the multivariate analysis.

#### 3.7 VALIDITY AND RELIABILITY

Validity, as defined by Taherdoost (2016), pertains to the extent to which a measurement accurately assesses what it is intended to measure. In Zambia's ART programme, standardised HIV management forms and the EMR are employed to systematically document clinical, pharmacy, and laboratory data, thereby ensuring consistency and validity. These data are recorded and entered by trained clinical, pharmacy, laboratory, and data entry clerks in both

the standardised forms and the EMR at the clinic. Regular data quality audits are conducted by the MOH and implementing partners to verify the accuracy and completeness of the data recorded on the standardised forms and the EMR. In this study, a specific query was executed on the EMR to collect data relevant to the research area, reducing measurement bias. Selection bias was mitigated by clearly defining the inclusion and exclusion criteria for the study population.

Reliability, as outlined by Taherdoost (2016), refers to the extent to which a measurement yields consistent and reproducible results for a given phenomenon. The utilisation of a standardised query and reports to extract data from the EMR ensured reliability. Once the query was executed on the EMR, the extracted data was exported to an Excel spreadsheet.

#### 3.8 ETHICS CONSIDERATIONS

Ethics clearance was obtained from the Biomedical Research Ethics Committee at the University of the Western Cape (Appendix 1: BM22/9/6), the Biomedical Ethics Committee at Mulungushi University (Appendix 2: SMHS-MU3-2022-14), and the National Health Research Authority (Appendix 3: NHRA0000001/04/09/2022). Permission to access the data from the EMR was granted by the Livingstone District Health Office (Appendix 4). Informed consent was not sought as patient-level data was extracted from the EMR, and direct contact with the patients was unnecessary. The Excel spreadsheet used for data extraction and analysis was protected by a password. To maintain patient anonymity, no patient names or identifiers were recorded in any study materials. All records utilised during and after the study were stored on password-protected storage devices, accessible solely to the researcher, and will be retained for a period of five years.

Given the retrospective nature of the data collected from the EMR, no health care interventions were recommended for the participating patients. Throughout the study, compliance with the regulations outlined in the Protection of Personal Information Act (POPIA, 2019) was strictly observed.

### **CHAPTER 4: RESULTS**

#### 4.1 INTRODUCTION

The previous chapter discussed the research methodology employed in this study. This chapter will focus on the results of the study.

#### 4.2 CHARACTERISTICS OF STUDY PARTICIPANTS

Table 4.1 presents the socio-demographic, clinical, treatment, and behavioural characteristics of adults residing with HIV who were registered to receive ART at Mahatma Gandhi Clinic as of August 2022. The majority of patients enrolled for ART at Mahatma Gandhi Clinic during the study period were aged between 30 and 49 years, comprising over 65% of the total. Specifically, the 30–39-year and 40–49-year age groups constituted 32.3% (n = 716) and 33.2% (n = 737), respectively. Females outnumbered males in ART enrolment, accounting for 65.1% compared to 34.9% at the clinic. Approximately two-thirds of the participants (64.1%; n = 1,418) were classified as married, divorced, or widowed, while 13.6% (n = 302) were recorded as single. Marital status information was not available for 297 participants (22.4%).

The majority of people living with HIV (PLHIV) registered for ART at Mahatma Gandhi Clinic had prior treatment experience, with over five years on ART constituting 76.3% (n = 1,692) of the total. Additionally, 21.4% (n = 475) and 2.3% (n = 50) had been receiving treatment for 3–5 years and 1–2 years, respectively. Furthermore, 68.7% (n = 1,522) had a documented WHO clinical stage, with the majority classified as stage I (94%; n = 1,432).

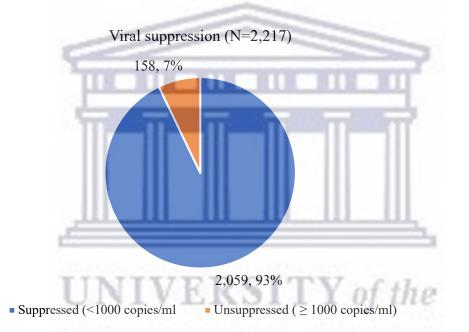
Just under half of the participants (46.5%, n = 1,031) displayed mild immune suppression, with a CD4 count slightly above 350 cells/mm<sup>3</sup> at the initiation of ART. Meanwhile, 9.7% (n = 216) exhibited moderate immune suppression (CD4 count < 200–350 cells/mm<sup>3</sup>), and 4.4% showed severe immune suppression with a CD4 count below 200 cells/mm<sup>3</sup>. CD4 count results were not available for 39.4% (n = 873) of the participants.

Conversely, among participants with a documented latest CD4 count, 30.2% (n = 670) displayed mild immune suppression (CD4 >350), with 16.3% (n = 361) experiencing moderate immune suppression (CD4 200–349 cells/mm<sup>3</sup>) and 15.6% (n = 346) demonstrating severe

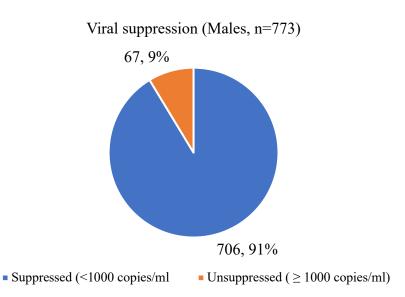
immune suppression. CD4 count results were not available for 37.9% (n = 840) of the participants.

The majority of PLHIV (97.1%; n = 2,153) were on the first-line regimen and had undergone a change in regimen since initiation (93.1%; n = 2,065). A small proportion of patients (1.7%; n = 38) had a reported history of tuberculosis (TB). Of the PLHIV, 79.2% (n = 1,755) had received TB prophylaxis.

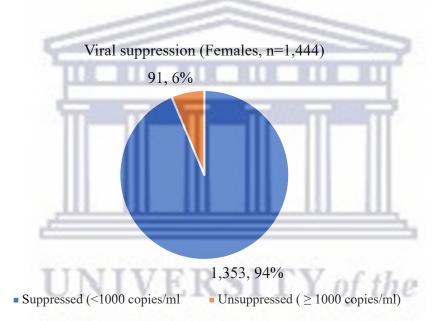
For most participants (93.1%; n = 2,064), optimal adherence was recorded in the three days leading up to the next drug refill, and they remained in care (81.7%; n = 1,930). Most (92.9%; n=2,059) of the participants were completely suppressed (< 1000 copies/ml); while 7.1% (n=158) were unsuppressed ( $\geq$  1000 copies/ml) (Figure 4.1).



**Figure 4.1**: Levels of viral suppression of adults registered for ART at a primary health care facility (N=2,217).



**Figure 4.2**: Levels of viral suppression of males registered for ART at a primary health care facility (n=773).



**Figure 4.3**: Levels of viral suppression of females registered for ART at a primary health care facility (n=1,444).

	Frequency (n)	Percentage (%)
Age group (in years)	- • · /	
< 20	125	5.6
20–29	272	12.3
30–39	716	32.3
40–49	737	33.2
50+	367	16.6
Gender		
Male	773	34.9
Female	1,444	65.1
Marital status		
Single		
Married	302	13.6
Widowed	990	44.7
Divorced	194	8.8
Missing	234	10.6
-	497	22.4
<b>Duration on ART</b> (in years)		
<1	0	0
1–2	50	2.3
3–5	475	21.4
> 5	1,692	76.3
Current WHO clinical stage		
1	1,432	64.6
2	46	2.1
3	34	1.5
4	10	0.5
Missing	695	31.3
Baseline CD4 count (cells/mm <sup>3</sup> )		
< 200	97	4.4
200–350	216	9.7
> 350	1,031	46.5
Missing	873	39.4
Latest CD4 count (cells/mm <sup>3</sup> )		
< 200	346	15.6
200–350	361	16.3
> 350	670	30.2
Missing	840	37.9
Most recent Viral load (copies/ml)	Uni D	
< 1000 (suppressed)	2,059	92.9
≥1000 (unsuppressed)	158	7.1
Current ARV regimen		
First-line	2,153	97.1
Second-line	64	2.9
Second-Infe		-
Change in ARV regimen Yes	2,065	93.1

Table 4.1: Social-demographic, clinical, treatment, and behavioural characteristics of adults registered for ART at primary health care facility: 2020-2022 (N = 2,217)

History of active TB			
Yes	38	1.7	
No	2,179	98.3	
Ever initiated on TB prophylaxis			
Yes	1,755	79.2	
No	0	0	
Unknown	462	20.8	
Optimal adherence in the last 3 days			
Yes	2,064	93.1	
No	153	6.9	
Retention in care			
Yes	1,930	87.1	
No	286	12.9	



http://etd.uwc.ac.za

#### 4.3 DETERMINANTS OF VIRAL SUPPRESSION

The results of the bivariate analysis on socio-demographic, clinical treatment, and behavioural characteristics associated with viral suppression are presented in Table 4.2.

#### 4.3.1 Socio-demographic factors

Table 4.2 indicates that viral suppression exhibited a statistically significant association with the socio-demographic factors, age (p = 0.02) and gender (p = 0.039). However, after adjusting for other variables, no significant association was observed between viral suppression and age (refer to Table 4.3). Regarding the association between viral suppression and gender, the analysis revealed that females had 41% higher likelihood of achieving viral suppression compared to males (crude odds ratio (OR) = 1.41; 95% CI = 1.02–1.96) (refer to Table 4.3). Nonetheless, this association **did not** retain its significance after controlling for all other variables in the multivariate logistic regression (adjusted OR (AOR) = 1.80; 95% CI = 0.95–3.39).

No statistically significant association was found between viral suppression and marital status (p = 0.392) (refer to Table 4.2).

## 4.3.2 Clinical factors

Table 4.2 reveals statistically significant associations between viral suppression and various clinical factors, including duration on ART (p < 0.001), CD4 count at ART initiation (p = 0.001), and latest CD4 count (p = 0.03).

Comparatively, individuals on ART for 3–5 years and over 5 years exhibited three-fold (OR = 3.63; 95% CI = 1.91-6.93) and ten-fold (OR = 10.12; 95% CI = 5.41-18.91) higher odds of viral suppression, respectively, in contrast to HIV patients on ART for 1-2 years (refer to Table 4.3). However, in the multivariate logistic regression, the relationship between viral suppression and duration on ART **did not** retain statistical significance.

A significant association was observed between viral suppression and CD4 count at ART initiation. In the bivariate analysis, individuals with CD4 counts between 200–350 cells/mm<sup>3</sup> (moderate immune suppression) and over 350 cells/mm<sup>3</sup> (mild immune suppression) demonstrated approximately three-fold (OR = 2.71; 95% CI = 1.39–5.28) and seven-fold (OR = 6.85; 95% CI = 3.84–12.20) higher odds of viral suppression, respectively, compared to those

with CD4 counts below 200 cells/mm<sup>3</sup> (severe immune suppression) (refer to Table 4.3). This association remained significant even after adjusting for all other variables in the multivariate logistic regression (AOR = 4.35; 95% CI = 1.61-11.75; AOR = 6.46; 95% CI = 2.44-17.08). Furthermore, a statistically significant association between viral suppression and the latest CD4 count (p = 0.03) was found, with individuals having a CD4 count above 350 cells/mm<sup>3</sup> having double the odds of achieving viral suppression compared to those with a CD4 count below 200–350 cells/mm<sup>3</sup> (OR = 2.02; 95% CI = 1.18-3.47) (refer to Table 4.3). However, this association **did not** retain statistical significance after adjusting for all other variables in the multivariate logistic regression (AOR = 1.16; 95% CI = 0.42-2.93).

No statistically significant association was identified between viral suppression and a history of active tuberculosis (p = 0.145) (refer to Table 4.2).

## 4.3.3 Treatment factors

Table 4.2 reveals statistically significant associations between viral suppression and treatment factors, including current antiretroviral (ARV) regimen (p < 0.001), change in ARV regimen (p < 0.001), and ever being initiated on tuberculosis (TB) prophylaxis (p < 0.001).

The association between current ARV regimen and viral suppression was statistically significant, indicating that individuals on the second-line regimen had 79% lower likelihood of achieving viral suppression compared to those on the first-line regimen (OR = 0.21; 95% CI = 0.12-0.38) (refer to Table 4.3). This association remained significant even after adjusting for all other variables in the multivariate logistic regression (AOR = 0.11; 95% CI = 0.04-0.31). In the bivariate analysis, individuals who had no change to a more efficacious ARV regimen exhibited 83% reduced odds of viral suppression compared to those who had a change to a more efficacious ARV regimen (OR = 0.17; 95% CI = 0.11-0.26) (refer to Table 4.3). The association remained significant after adjusting for all other variables in the multivariate logistic for all other variables in the multivariate logistic segression (AOR = 0.11-0.26) (refer to Table 4.3). The association remained significant after adjusting for all other variables in the multivariate logistic regression (AOR = 0.30; 95% CI = 0.11-0.78).

Furthermore, viral suppression showed a statistically significant association with *ever being initiated on TB prophylaxis*. Individuals who were never initiated on TB prophylaxis had 64% lower odds of achieving viral suppression compared to those who had *ever been initiated on TB prophylaxis* (OR = 0.36; 95% CI = 0.26-0.51) (refer to Table 4.3). However, this

association **did not** retain statistical significance after adjusting for all other variables in the multivariate logistic regression (AOR = 0.69; 95% CI = 0.35-1.33).

#### 4.3.4 Behavioural factors

Table 4.2 demonstrates statistically significant associations between viral suppression and behavioural factors, including optimal adherence in the last three days (p < 0.001) and retention in care (p < 0.001).

The association between viral suppression and optimal adherence in the last three days was statistically significant. Individuals who were not optimally adherent had 77% lower odds of achieving viral suppression compared to those who were optimally adherent in the last three days (OR = 0.23; 95% CI = 0.15-0.36) (refer to Table 4.3). This association remained significant after adjusting for all other variables in the multivariate logistic regression (AOR = 0.41; 95% CI = 0.18-0.95).

Lastly, viral suppression and retention in care also showed a statistically significant association. Individuals who were not retained in care had 82% lower odds of achieving viral suppression compared to those who were retained in care (OR = 0.18; 95% CI = 0.13-0.25) (refer to Table 4.3). This association remained significant after adjusting for all other variables in the multivariate logistic regression (AOR = 0.23; 95% CI = 0.12-0.46).



	•	Total	Viral load	<u>e facility in Living</u> Viral load	p-value
		Iotai	< 1000 n (%)	$\geq 1000 \text{ n} (\%)$	p value
Age (in years)	< 20	125	113 (90.4)	12 (9.6)	0.022
Age (III years)	< 20 20–29	272	242 (89)	. ,	0.022
				30 (11)	
	30-39	716	662 (92.5)	54 (7.5)	
	40-49	737	695 (94.3)	42 (5.7)	
	50+	367	347 (94.6)	20 (5.4)	
Gender	Male	773	706 (91.3)	67 (8.7)	0.039
	Female	1,444	1,353 (93.7)	91 (6.3)	
Marital status (n = 1,720)	Single	302	273 (90.4)	29 (9.6)	0.392
	Married	990	927 (93.6)	63 (6.4)	
	Divorced	234	219 (93.6)	15 (6.4)	
	Widowed	194	181 (93.3)	13 (6.7)	
	Widowed	174	101 (55.5)	15 (0.7)	
<b>Duration on ART</b> (in years)	1–2	50	33 (66)	17 (34)	< 0.001
	3–5	475	416 (87.6)	59 (12.4)	
	> 5	1,692	1,610 (95.2)	82 (4.8)	
Current WHO clinical stage	1	1,432	1,360 (95)	72 (5)	0.832
6		,			0.852
(n = 1,522)	2	46	44 (95.7)	2 (4.3)	
11.8	3	34	33 (97.1)	1 (2.9)	
	4	10	9 (90)	1 (10)	
Baseline CD4 at initiation	< 200	97	76 (78.4)	21 (21.6)	< 0.001
$(cells/mm^3)$ (n = 1,344)	200-350	216	196 (90.7)	20 (9.3)	
	> 350	1,031	991 (96.1)	40 (3.9)	
Latest CD4 count (cells/ mm <sup>3</sup>	< 200	346	318 (91.9)	28 (8.1)	0.03
	200–350	361		· · ·	0.05
(n = 1,377)			337 (93.4)	24 (6.6)	
1.1	> 350	670	642 (95.8)	28 (4.2)	
Current ARV regimen	First-line	2,153	2,016 (93.6)	137 (6.4)	< 0.001
TINI	Second-	64	51(79.6)	13 (20.4)	
Change in ARV	line Yes	2,059	1,947 (94.3)	118 (5.7)	< 0.001
5		,		· · ·	< 0.001
regimen	No	152	112 (73.7)	40 (26.3)	
History of active TB	Yes	38	33 (86.8)	5 (13.2)	0.145
	No	2,179	2,026 (93)	153 (7)	
Ever initiated on TB	Yes	1,755	1,660 (94.6)	95 (5.4)	< 0.001
prophylaxis	No	462	399 (86.4)	63 (13.6)	
Optimal adherence for the	Yes	2,064	1,939 (93.9)	125 (6.1)	< 0.001
last 3 days	No	153	120 (78.4)	33 (21.6)	× 0.001
lasi 5 uays	INU	155	120 (70.4)	55 (21.0)	
Retention in care	Yes	1,930	1836 (95.1)	94 (4.9)	
	No	287	223 (77.7)	64 (22.3)	< 0.001

 Table 4.2: Bivariate analysis of viral suppression by socio-demographic, clinical, treatment, and behavioural characteristics of ART patients at a primary health care facility in Livingstone

	TOTAL	Crude OR	95% CI	Adjusted OR	95% CI
Age (in years)				~	
< 20	125	Ref			
20–29	272	0.86	0.42-1.76	0.89	0.20-3.93
30–39	716	1.30	0.68-2.51	1.15	0.28-4.67
40-49	737	1.76	0.90-3.44	0.97	0.23-4.03
> 50	367	1.84	0.87-3.89	1.16	0.26–5.30
Gender					
Male	773	Ref		Ref	
Female	1,444	1.41	1.02-1.96	1.80	0.95-3.39
Duration on ART	(in years)				
1–2	50	Ref		Ref	
3–5	475	3.63	1.91-6.93	1.00	0.20-5.09
> 5	1,692	10.12	5.41-18.91	1.41	0.25-7.94
Baseline CD4 at ir	· · · · · · · · · · · · · · · · · · ·				
(in cells/mm <sup>3</sup> )					
< 200	97	Ref		Ref	
< 200–350	216	2.71	1.39-5.28	4.35	1.61-11.75
> 350	1,031	6.85	3.84-12.20	6.46	2.44-17.08
	TIM	IN BIN			
Latest CD4 count	100				
in cells/ mm <sup>3</sup> )	-		1000	ALC: NO.	
< 200	346	Ref	- 10- 0	Ref	
< 200–350	361	1.24	0.70-2.18	0.59	0.25-1.38
> 350	670	2.02	1.18–3.47	1.16	0.42-2.93
Current ARV					
regimen			111 11		
First-line	2,153	Ref		Ref	
Second-line	64	0.21	0.12-0.38	0.11	0.04-0.31
Change in ARV ro		VED	SITT	T a f sha	
Yes	2,065	Ref	3111	Ref	
No	152	0.17	0.11-0.26	0.30	0.11-0.78
Ever initiated on T prophylaxis	вЕ	STEP	RN C	APE	
Yes	1,930	Ref		Ref	
No	287	0.36	0.26-0.51	0.69	0.35-1.33
Optimal adherenc	e for the last	3 davs			
Yes	2,064	Ref		Ref	
No	153	0.23	0.15-0.36	0.41	0.18-0.95
<b>Retention in care</b>					
Yes	1,930	Ref		Ref	
	,	-		-	0.12-0.46

Table 4.3: Determinants of viral suppression of PLHIV on ART at a primary health care facility in Livingstone, 2020–2022

#### 4.4 DETERMINANTS OF RETENTION IN CARE

This section will consider determinants of retention in care. As of August 2022, retention in care for adults registered for ART at a primary health care facility was at 87.1% (retained).

#### 4.4.1 Socio-demographic factors

In the bivariate analysis, retention in care exhibited a statistically significant association with age (p < 0.001), as indicated in Table 4.4. However, as shown in Table 4.3, this association **did not** retain statistical significance after adjusting for all other variables in the multivariate logistic regression. There were no statistically significant associations found between viral suppression and gender (p = 0.902) or marital status (p = 0.404) (refer to Table 4.4).

#### 4.4.2 Clinical factors

Table 4.4 demonstrates that retention in care was statistically significantly associated with *duration on ART* (p < 0.001) and viral suppression (p < 0.0001).

Compared to HIV patients on ART for 1–2 years, those on ART for 3–5 years and over 5 years had four-fold (OR = 4.34; 95% CI = 2.38-7.91) and approximately nine-fold (OR = 8.78; 95% CI = 4.94-15.62) higher odds of being retained in care, respectively (refer to Table 4.5). In the multivariate logistic regression, the odds of being retained in care remained significant only for those on ART for over five years (AOR = 2.35; 95% CI = 1.09-5.05) in comparison to those on ART for 1–2 years.

HIV patients with non-suppressed viral load ( $\geq 1000$  copies/ml) had an 82% lower odds of being retained in care compared to those with viral suppression (< 1000 copies/ml) (OR = 0.18; 95% CI = 0.13-0.25) (refer to Table 4.5). After adjusting for all other variables in the multivariate logistic regression, the odds of being retained in care slightly increased but remained protective for patients who were not virally suppressed (AOR = 0.33; 95% CI = 0.22-0.48).

No statistically significant associations were found between retention in care and current WHO clinical stage (p = 0.708), CD4 count at ART initiation (p = 0.078), latest CD4 count (p = 0.326), and a history of active tuberculosis (p = 0.654) (refer to Table 4.4).

## 4.4.3 Treatment factors

Table 4.4 reveals that retention in care exhibited statistically significant associations with treatment factors, including change in antiretroviral (ARV) regimen (p < 0.001) and ever being initiated on tuberculosis (TB) prophylaxis (p < 0.001).

In the bivariate analysis, individuals who had no change to a more efficacious ARV regimen had an 80% lower odds of being retained in care compared to those who had a change to a more efficacious ARV regimen (OR = 0.20; 95% CI = 0.14-0.29) (refer to Table 4.5). This association remained significant after adjusting for all other variables in the multivariate logistic regression (AOR = 0.38; 95% CI = 0.23-0.62).

Similarly, individuals who were never initiated on TB prophylaxis had an 84% lower odds of being retained in care compared to those who had been initiated on TB prophylaxis (OR = 0.36; 95% CI = 0.26–0.51) (refer to Table 4.3). This association retained its significance even after adjusting for all other variables in the multivariate logistic regression (AOR = 0.37; 95% CI = 0.28–0.50). No statistically significant association was found between retention in care and current ARV regimen (p = 0.517) (refer to Table 4.4).

## 4.4.4 Behavioural factors

Table 4.4 demonstrates that retention in care was statistically significantly associated with the behavioural factor of optimal adherence in the last three days (p < 0.001). Individuals who were not optimally adherent had a 77% lower odds of achieving viral suppression compared to those who were optimally adherent in the last three days (OR = 0.23; 95% CI = 0.15–0.36) (refer to Table 4.3). This association remained significant after adjusting for all other variables in the multivariate logistic regression (AOR = 0.41; 95% CI = 0.18–0.95).



	*		Data in al	•		
		Retained in care Total Yes No			p-value	
		Total	n (%)	n (%)	p-value	
Age (in years)	< 20	125	109 (87.2)	16 (12.8)	< 0.001	
Age (in years)	20–29	272	209 (76.8)	63 (23.2)	< 0.001	
	20–29 30–39	716	612 (85.5)	· · · ·		
				104(14.5)		
	40-49	737	673 (91.3)	64 (8.7)		
	50+	367	327 (89.1)	40 (10.9)		
Gender	Male	733	672 (86.9)	101 (13.1)	0.902	
	Female	1,444	1,258 (87.1)	186 (12.9)		
Marital status (n = 1,720)	Single	302	256 (84.9)	46 (15.2)	0.404	
(i 1,,20)	Married	990	822 (83)	168 (17)	0.101	
	Divorced			· · ·		
		234	209 (89.6)	25 (10.4)		
	Widowed	194	172 (88.7)	22 (11.3)		
Duration on ART	< 1	0	0 (0)	0 (0)	< 0.001	
in years)	1–2	50	25 (50)	25 (50)		
	3–5	475	386 (81.3)	174 (18.7)		
	> 5	1,692	1,346 (73.6)	346 (20.4)		
1000		1,072	1,0 10 (7010)	0.00 (2000)		
Current WHO clinical	-1	1432	1,283 (89.6)	149(10.4)	0.708	
stage (n = 1,522)	2	46	40 (87)	6 (13)		
	3	34	31 (91.2)	3 (8.8)		
110	4	10	8 (80)	2 (20)		
		10	0 (00)	2 (20)		
Baseline CD4 count	< 200	97	84 (86.6)	13 (13.4)	0.078	
in cells/ mm <sup>3</sup> ) (n = 1,344)	200-350	216	184 (85.2)	32 (14.9)		
	> 350	1,031	929 (90.1)	102 (9.9)		
سالللى .	- 550	1,051	929 (90.1)	102 (9.9)		
Latest CD4 count	< 200	346	311 (89.9)	35 (10.1)	0.326	
in cells/ mm <sup>3</sup> ) (n = 1,377)	200-350	361	329 (88.4)	32 (11.6)		
, ( ))	> 350	670	1 (86.7)	89 (10)		
Current ARV regimen	First-line	2,153	1,876 (87.1)	277 (12.9)	0.517	
Current AKy regimen	Second-	,			0.517	
TAT T	line	64	54 (84.4)	10 (15.6)		
VY L	DI.	I. I.	IN CULT	1 12		
Change in ARV regimen	Yes	2,065	1,836 (88.9)	229 (11.1)	< 0.001	
	No	152	94 (61.8)	58 (38.2)		
History of active TB	Yes	38	34 (89.5)	4 (11.5)	0.654	
Level of active 1D	No	2,179	1,896 (87)	283 (13)	0.001	
	110	2,177	1,070 (07)	205 (15)		
Ever initiated on TB	Yes	1,755	1,586 (90.4)	169 (9.6)	< 0.001	
prophylaxis	No	462	344 (74.4)	118 (25.6)		
		-				
Optimal adherence in the	Yes	2,064	1,842 (89.2)	222 (11.8)	< 0.001	
ast 3 days	No	153	88 (57.5)	65 (42.5)		

 Table 4.4: Bivariate analysis of retention in care by socio-demographic, clinical treatment, and behavioural characteristics of ART patients at a primary health care facility in Livingstone

		Retained in care			
		Total	Yes n (%)	No n (%)	p-value
Viral load suppression	Yes (< 1000)	2,059	1,836 (89.2)	223 (11.8)	< 0.001
(copies/ml)	No (≥1000)	158	94 (59.5)	64 (40.5)	

Table 4.5: Determinants of retention in care of PLHIV on ART at Mahatma Gandhi clinic in Livingstone, 2020–2022

	TOTAL	Crude OR	95% CI	Adjusted OR	95% CI
Age					
< 20	125	Ref		Ref	
20–29	272	0.49	0.27-0.88	0.56	0.29-1.09
30–39	716	0.86	0.49-1.52	0.83	0.45-1.56
40–49	737	1.54	0.86-2.77	1.21	0.64-2.31
> 50	367	1.20	0.65-2.23	0.89	0.45-1.76
<b>Duration on</b>					
ART (in years)					
1–2	50	Ref		Ref	
3–5	475	4.34	2.38-7.91	1.87	0.91-3.83
> 5	1692	8.78	4.94–15.62	2.35	1.09-5.05
Change in ARV					
regimen					
Yes	2,065	Ref		Ref	
No	152	0.20	0.14-0.29	0.38	0.23-0.62
Ever initiated on					
TB prophylaxis					
Yes	1,930	Ref	SITV	Ref	
No	287	0.31	0.24-0.40	0.37	0.28-0.50
Optimal					
adherence in the	AT TT 6	CONTROL 1	DATC	ADE	
last 3 days	W LO		NIN U.	AFE	
Yes	2,064	Ref		Ref	
No	153	0.16	0.12-0.23	0.25	0.17-0.37
Viral suppression	1				
< 1000	2,059	Ref		Ref	
≥1000	158	0.18	0.13-0.25	0.33	0.22-0.48

# **CHAPTER 5: DISCUSSION**

# 5.1 INTRODUCTION

The preceding chapter focused on the results of the study. This chapter provides an analysis of the research findings in connection with the study objectives and existing literature. The discussion is structured into the subsequent subsections: summary characteristics of the adult HIV population receiving treatment; treatment outcomes, specifically viral suppression and retention in care; depiction of adherence and identification of risk factors influencing ART adherence among patients utilising ART services at a primary health care facility in Livingstone amidst the COVID-19 pandemic.

# 5.2 PROFILE OF THE ADULT HIV POPULATION ON TREATMENT

The adult HIV population receiving treatment in this investigation was predominantly female (65.1%). This aligns with comparable research conducted in Zimbabwe (Takarinda *et al.*, 2015), South Africa (Human Sciences Research Council, 2017), and Ghana (Abubakari *et al.*, 2023), and is in line with the global trend where 80% of female adults aged 15 years and older had access to treatment compared to 70% of male adults aged 15 years and older (UNAIDS, 2022).

The majority of the study cohort exhibited a baseline CD4 count exceeding 350 cells/mm<sup>3</sup>. This observation can be attributed to the modification in Zambia's national guidelines for ART initiation eligibility criteria (MOH, 2010), which raised the threshold for ART eligibility to a CD4 count of less than 500 cells/mm<sup>3</sup>. Moreover, most of the participants had been receiving ART for a period surpassing three years. This finding is consistent with a study carried out in Ghana, where over half of the adult population on ART had been undergoing treatment for more than three years (Abubakari *et al.*, 2023). Additionally, similar investigations conducted in Kenya (Mugo *et al.*, 2022) and Ethiopia (Tegegne, 2021) indicate that an extended duration of ART positively impacts the CD4 count (Aavani & Allen, 2019).

## 5.2.1 Viral suppression

The achievement of the UNAIDS 90-90-90 targets, which advocate for 90% of people living with HIV (PLHIV) to attain a viral suppression rate of 90% while on ART (UNAIDS, 2014), is a significant milestone. In this study, the researcher reports a viral suppression rate of 92.9%

among the adult population, surpassing the UNAIDS target. However, it falls short of the adjusted UNAIDS 95-95-95 targets (UNAIDS, 2015). Similar to the findings of this study, Rwanda, Botswana, Uganda, and Malawi have successfully achieved the UNAIDS 90-90-90 targets, while Eswatini has achieved slightly over 86% viral suppression for all PLHIV (Frescura *et al.*, 2022). In contrast, a study conducted in Cameroon by Fokam *et al.* (2019) reported a much lower viral suppression rate of only 79.4% among PLHIV on ART. The attainment of viral suppression is influenced by various factors, including individual, societal, and structural barriers that specific populations encounter in accessing health care services (Ayala *et al.*, 2021).

#### 5.2.2 WHO clinical stage at initiation of HIV treatment

The majority of the adult HIV population currently receiving ART in this study were asymptomatic and categorised as WHO clinical stage 1. This observation can be attributed to the adoption of the universal test-and-treat strategy and the consequent slow progression of immunosuppression as outlined in the national guidelines (MOH, 2020). Most countries in sub-Saharan Africa, including Southern Africa, have embraced the universal test-and-treat strategy (WHO, 2017). Consistent with the findings of this study, a study conducted at Komfo Anokye Teaching Hospital (KATH) in Ghana revealed that the majority of patients receiving ART were classified as WHO clinical stage I (Opoku *et al.*, 2022).

#### 5.2.3 Prevalence of HIV-TB co-infection

It is well-established that HIV-TB co-infection significantly impacts the prognosis of both diseases. HIV infection is a strong predictor of TB infection and disease (Dye *et al.*, 2006; Karim *et al.*, 2010). In this study, a substantial proportion of the adult HIV population receiving ART had no history of active TB. This finding can be attributed to the evidence demonstrating that the combined use of Isoniazid Preventive Treatment (IPT) and ART can lead to up to a 90% reduction in the overall incidence and mortality of TB, with ART alone reducing the incidence of TB by up to 65% (Badje *et al.*, 2017; Person & Sterling, 2012). The majority (79%) of the adult HIV population in this study had a history of being initiated on TB prophylaxis, which could have acted as a preventive measure against acquiring active TB. However, these findings differ from a systematic review reported in the 2018 Global TB report, which highlighted the burden of TB in sub-Saharan Africa (SSA) due to the high prevalence of TB-HIV co-infection, with over 51% of TB cases being co-infected with HIV (WHO, 2018b).

## 5.2.4 HIV regimen characteristics

The majority of individuals in this study (> 90%) were prescribed the first-line regimen, with the remaining participants on the second-line regimen. According to national guidelines (MOH, 2022), the preferred first-line regimen for adults consists of Tenofovir (TDF), Lamivudine or Emtricitabine (3TC/FTC), and DTG. The preferred second-line regimen includes the Protease Inhibitor Lopinavir/Ritonavir (LPV/r) or alternatively Darunavir/Ritonavir (DRV/r). The shift from Efavirenz (EFV) to DTG in the national guidelines is based on factors such as reduced side effects, increased efficacy, and the ability to achieve viral suppression in a shorter time period (Affenito et al., 2012; DI Carlo et al., 2021; MOH, 2022). Reports indicate that after three months of treatment, 81% of patients on a DTG-based regimen achieved viral loads below 50 copies/ml, compared to 61% of patients on an EFV-based regimen (WHO, 2018a). With the majority of participants in this study receiving the first-line regimen, the high viral suppression rate above 90% among the adult HIV population supports the efficacy of DTG. Similar findings were reported in a study on factors related to HIV viral load suppression on antiretroviral therapy in Vietnam, where less than 4% of participants were on the second-line regimen, while the majority were on the first-line regimen (Rangarajan et al., 2016). The second-line regimen is primarily prescribed to individuals who show no signs of viral suppression after a second blood sample is collected and analysed following EAC (MOH, 2022).

> UNIVERSITY of the WESTERN CAPE

#### 5.2.5 Self-reported adherence to ART

The study revealed that the majority of patients (93.1%) on ART reported optimal adherence to their medication. This high adherence rate may be influenced by the policy guidance provided by the MOH, which allows for the dispensing of 3–6 months' worth of antiretrovirals (ARVs) to stable, virally suppressed patients (Pry *et al.*, 2022). It is important to note that the 93.1% adherence rate in this study may be lower than reported, as the electronic health record (EHR) system, based on dispensation, may inaccurately suggest adherence even if patients are not consistently taking their medication. Additionally, the reduction in ARV pill burden, with most PLHIV on ART taking only one tablet daily (MOH, 2022), may have positively influenced adherence. Similarly, studies conducted in Botswana, Senegal, and Nigeria reported high levels of adherence at 92.5%, 91%, and ≥95%, respectively (Bastard *et al.*, 2011; Bussmann *et al.*, 2010; Meloni *et al.*, 2016).

## 5.2.6 Retention in care to ART

This study revealed that nearly 90% of patients accessing services at the primary health care facility remained engaged in care as of August 2021. In response to the COVID-19 pandemic, various differentiated service delivery (DSD) models were implemented to ensure the continuous engagement of people living with HIV (PLHIV) who were receiving ART. Notably, the country adopted DSD models such as community-based ARV dispensation, fast-track approaches, and multi-month scripting and dispensation (providing a 3–6 months' supply of drugs) (Jo *et al.*, 2021). These models likely contributed to the high retention rates observed during the COVID-19 pandemic in this study. Similar findings regarding retention rates were reported in a study conducted in South Africa, where PLHIV enrolled in DSD models demonstrated retention rates of 96%, 93%, and 90% at 12, 24, and 36 months, respectively (Shigayeva *et al.*, 2022).

42

#### 5.3 DETERMINANTS OF VIRAL SUPPRESSION

This study identified several factors that showed statistical significance in the bivariate analysis. However, the multivariate analysis revealed that only baseline CD4 count at initiation, current ARV regimen, change in ARV regimen, optimal adherence in the last three days, and retention in care had a significant impact on viral suppression.

Regarding gender, females exhibited a higher likelihood of viral suppression compared to males in this study. A systematic review and meta-analysis examining socio-demographic heterogeneity across the HIV treatment cascade and progress towards 90-90-90 in SSA found that, unlike in Botswana, males in Zambia were less likely than females to utilise ART, which is crucial for achieving viral suppression. This difference in ART usage by gender could explain the higher likelihood of viral suppression observed among females in this study. However, studies conducted in South Africa and Eastern Uganda did not find a significant association between gender and viral suppression (Boyer *et al.*, 2016; Gaolathe *et al.*, 2017; Grobler, 2017; Holmes *et al.*, 2018; Wakooko *et al.*, 2020). In contrast to the findings of this study, research by Azia *et al.* (2016) in South Africa and Desta *et al.* (2020) in Ethiopia reported that males were more likely to achieve viral load suppression than females.

The duration of ART was found to be significantly associated with viral suppression in this study. PLHIV who had been on ART for three or more years had 3.63 and 10.12 times increased odds of viral suppression compared to those on ART for 1–2 years. Similar findings were reported in South Africa (Berihun *et al.*, 2023; Haghighat *et al.*, 2021), Kenya (Cherutich *et al.*, 2016), and Ghana (Lokpo *et al.*, 2020), where a longer duration on ART was associated with a higher likelihood of viral suppression.

The findings of this study indicated that a higher baseline CD4 count was associated with an increased likelihood of achieving viral suppression among the adult HIV population. This aligns with the results reported by Bennett *et al.* (2002), Bonnet *et al.* (2005), and Grabar *et al.* (2005), who found that individuals initiating ART with moderate immune suppression (CD4 = 200-350 cells/mm<sup>3</sup>) or mild immune suppression (CD4 > 350 cells/mm<sup>3</sup>) had better virological outcomes compared to those with a CD4 count < 200 cells/mm<sup>3</sup>. Similar associations between higher CD4 count at ART initiation and improved viral suppression have also been observed in studies conducted in Tanzania (Muri *et al.*, 2017) and Nigeria (Abdullahi *et al.*, 2021). In previous years, patients' attitudes towards ART were influenced by clinical messaging that

emphasised the lack of necessity for ART among individuals with high CD4 counts. However, with the introduction of ART initiation regardless of CD4 count, patients' attitudes towards ART have become more positive, which could potentially contribute to this finding (Jain *et al.*, 2014).

The study identified a significant association between the current ARV regimen and the change in ARV regimen with viral suppression. The introduction of DTG in the first-line ARV regimen, as per the national guidelines, resulted in decreased odds of viral suppression among the adult HIV population on the second-line regimen compared to those on the first-line regimen. This finding is consistent with an epidemiological study conducted in Ghana, which reported higher viral suppression rates among patients on the first-line ART compared to those on other lines of treatment (Barry *et al.*, 2013).

Likewise, participants who did not experience a change in their ARV regimen had decreased odds of viral suppression compared to those who underwent a change in their ARV regimen (AOR = 0.30; 95% CI = 0.11-0.78). These results suggest that switching to a more effective ART regimen, such as DTG-based regimens, may have enhanced viral suppression. Similar findings have been reported in Ethiopia (Mehari *et al.*, 2021), Lesotho (Brown *et al.*, 2022), Uganda (Nabitaka *et al.*, 2020), as well as in Nigeria, Kenya, Uganda, and Tanzania (Esber *et al.*, 2022).

This study identified an association between TB prophylaxis and viral suppression, with individuals who had never initiated TB prophylaxis having reduced odds of achieving viral suppression compared to those who had ever initiated TB prophylaxis. The adult HIV population who had received TB prophylaxis demonstrated higher rates of viral suppression due to the preventive therapy reducing their risk of acquiring active TB, which in turn positively impacted their ability to achieve viral suppression (Getaneh *et al.*, 2022; Zanoni *et al.*, 2011). In HIV-infected individuals, the development of active TB has been linked to increased viral load (Goletti *et al.*, 1996). Similar findings to this study have been reported in Uganda (Toossi *et al.*, 2001).

This study also found an association between optimal adherence to antiretroviral medication (ART) and viral suppression. Maintaining adequate adherence to ART is crucial for PLHIV to achieve and sustain virological suppression (Byrd *et al.*, 2019; Umeokonkwo *et al.*, 2019).

Participants who were not optimally adherent to ART were less likely to achieve viral suppression compared to those who demonstrated optimal adherence. Similar findings have been reported in Rwanda, where a nationally representative study examined high levels of adherence and viral suppression among HIV-infected adults on ART for 6, 12, and 18 months (Elul *et al.*, 2013).

Retention in care was found to be associated with viral suppression in this study, aligning with research findings from Mugavero *et al.* (2012), Giordano *et al.* (2007), and Tripathi *et al.* (2011). Similar retention rates have been reported in Zimbabwe (Mutasa-Apollo *et al.*, 2014) and Nigeria (Onoka *et al.*, 2013) compared to the findings of this study. Retention in care is considered a marker of high-quality health care and is crucial for patients to experience viral suppression and other positive outcomes associated with HIV treatment (Umeokonkwo *et al.*, 2019).

# 5.4 DETERMINANTS OF RETENTION IN CARE

Duration on ART, change in ARV regimen, ever initiated on TB prophylaxis, optimal adherence in the last 3 days, and viral suppression were found to be statistically significant in the multivariate analysis of this study.

Regarding duration on ART, the findings revealed an association with retention in care, as individuals who had been on ART for more than 5 years had higher odds of being retained in care compared to those on ART for 1–2 years. This aligns with a systematic review on patient retention in antiretroviral therapy programmes in sub-Saharan Africa, which reported a greater likelihood of retention with longer duration on ART (Fox & Rosen, 2010). However, these findings differ from a study conducted in the DRC that found a negative association between length of time on ART and retention. Patients on ART for 7 months had over 7 times the odds of retention compared to those on ART for 53 months or longer (Shah *et al.*, 2022).

The study also identified an association between a change to a more efficacious ARV regimen and retention in care. However, this finding contradicts the study by Gumede *et al.* (2022), where the transition or change to TDF and DTG regimen showed no association with retention in care. The difference in findings can be attributed to the focus of this study, which aimed to introduce a more efficacious drug rather than solely reduce pill burden. In terms of TB prophylaxis, the study found an association with retention in care, with 90.4% of the adult HIV population who had ever received TB prophylaxis being retained in care. TB prophylaxis is known to reduce morbidity and mortality among PLHIV, preventing the development of active TB and subsequent disengagement from care (Melgar *et al.*, 2020). This finding aligns with similar reports in Cameroon (Tsague *et al.*, 2008) and North East Malaysia (Jalal *et al.*, 2017), where TB has been identified as a risk factor for poor outcomes and disengagement from HIV care in HIV clinics in sub-Saharan Africa and other less developed settings.

Optimal adherence was also associated with retention in care, as those who were not adherent had lower odds of being retained in care compared to those who demonstrated optimal adherence. Suboptimal retention in HIV care is known to be associated with poor ART adherence and suboptimal virologic suppression, leading to worsened health outcomes (Frieden *et al.*, 2019; Kakkar *et al.*, 2016).

# 5.5 SUMMARY

This study utilised viral suppression and retention in care as measures of adherence to ART in the adult HIV population at the primary health care facility. These measures are considered more objective and reliable compared to patient self-reports, questionnaires, surveys, and other methods (Tanyi *et al.*, 2021). Given the strong correlation between retention in care and medication adherence, factors influencing retention in care are likely to impact medication adherence and, consequently, viral load suppression. Nationally, viral suppression serves as a proxy indicator for assessing adherence among people living with HIV (PLHIV), although non-suppression does not necessarily imply non-adherence to medication (Wiener *et al.*, 2004).

Previously, there was a focus on intensified routine adherence during every clinic visit at the national level. However, the current approach involves implementing EAC or interventions only when PLHIV are found to have unsuppressed viral load results. In line with the Zambia Consolidated ART national guidelines (MOH, 2020), the process of engaging PLHIV with unsuppressed viral load results to achieve viral suppression is referred to as EAC. Unscheduled adherence sessions are conducted, and the quantity of medication dispensed to individuals with unsuppressed viral load is reduced to facilitate the adherence sessions. After three months, a fresh blood sample is collected for viral load determination.

# **CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS**

# 6.1 INTRODUCTION

The penultimate chapter was a discussion on the results of the study. This final chapter considers the conclusion, limitations, and recommendations of the study.

# 6.2 CONCLUSIONS

This study aimed to identify risk factors associated with viral suppression and retention in care among adults with HIV receiving ART. Gender, duration on ART exceeding three years, CD4 count at baseline ranging from 200 to 350 cells/mm<sup>3</sup>, CD4 count greater than 350 cells/mm<sup>3</sup> at the latest assessment, current ARV regimen, switch to a more effective ARV regimen, initiation of tuberculosis (TB) prophylaxis, optimal adherence to ART in the last three days, and overall retention in care showed significant associations with viral suppression. Regarding retention in care, significant associations were observed with duration on ART exceeding three years, switch to a more effective ARV regimen, initiation of TB prophylaxis, optimal adherence to ART in the last three days, and viral suppression. These associations identified in the study could be incorporated into the design of adult ART programmes and tailored interventions. To further explore barriers to retention in care and viral load suppression, and to inform the development of targeted interventions and programmes, additional research using qualitative study designs would be necessary to expand our understanding of these issues.

In Zambia, pill counts and self-reports are no longer considered reliable methods for assessing adherence to ART. As an alternative, the next scheduled ARV drug refill appointment date is being used as a proxy method for adherence measurement. However, this approach is also prone to inaccuracy since patients may obtain their ARV drug refills from a different facility without informing their original facility of access. In response to this challenge, viral load monitoring has become a routine practice for measuring adherence. Regular viral load monitoring is considered essential and cost-effective, as it offers good specificity and sensitivity in identifying poor adherence to ART and detecting treatment failure among people living with HIV (PLHIV) (Barnabas *et al.*, 2017; Glass *et al.*, 2020). PLHIV with unsuppressed viral load results are offered EAC for an initial three-month period to determine whether the unsuppressed results are due to suboptimal adherence (Bvochora *et al.*, 2019; Kaira *et al.*, 2021;

MOH, 2020). Consequently, apart from viral load and retention in care, our study was unable to measure adherence or provide a comprehensive report on indicators of poor adherence.

# 6.3 LIMITATIONS OF THE STUDY

The primary limitation of this study pertains to the absence of records in the data extracted from the EMR system. Missing values for each variable were excluded, and the analysis was conducted based on complete records only. This omission may have influenced the analysis of variables associated with viral suppression and retention in care. As the health care institution solely relies on electronic records for the provision of ART services, data extraction from the EMR was necessary for the specified study period. Consequently, the researcher was unable to verify missing variables subsequent to their extraction from the EMR. Moreover, the utilisation of the extracted data constrained the extent to which additional variables, such as social, cultural, religious, and economic factors, which were not captured in the EHR, could exert an influence on viral suppression and retention in care.

# 6.4 **RECOMMENDATIONS**

The recommendations that follow are intended to inform programmatic approaches to improve viral suppression and retention in care.

# 6.3.1 Interventions to address identified risk factors

This sub-section deals with recommendations regarding socio-demographic factors, clinical factors, treatment factors, and behavioural risk factors.

# 6.3.1.1 Socio-demographic factors

Considering the notable association between viral suppression and gender, programme design should incorporate interventions tailored to engage both males and females in treatment programmes. These initiatives may involve targeted campaigns, community-based events, and gender-specific peer support groups.

#### 6.3.1.2 Clinical factors

As evidenced by the study, the duration of ART exhibited a significant association with viral suppression and retention in care. Programme design should integrate strategies to ensure that people living with HIV (PLHIV) who initiate ART remain on treatment for their lifetime. This can be achieved through a patient-centred approach that prioritises the needs and concerns of

PLHIV. Active involvement of patients in the development of their care plan and addressing any barriers to adherence will be essential.

The study also revealed that viral suppression was associated with baseline CD4 counts between 200 and 350 cells/mm<sup>3</sup>, as well as counts exceeding 350 cells/mm<sup>3</sup>, with the latest CD4 count exceeding 350 cells/mm<sup>3</sup>. However, with the shift towards treating all PLHIV regardless of CD4 count, the programme must ensure prompt initiation of ART for all PLHIV before they reach a state of immunocompromise (Nicol *et al.*, 2022).

#### 6.3.1.3 Treatment factors

According to the study, viral suppression exhibited a significant association with the current antiretroviral (ARV) regimen, while both viral suppression and retention in care were significantly associated with switching to a more efficacious ARV regimen. Programme design should ensure that all PLHIV are initiated on the most appropriate combination of ARV regimens, considering their specific contraindications. Additionally, priority should be given to switching those who are not on the most effective regimen that maximises viral suppression (Esber *et al.*, 2022).

Furthermore, the study demonstrated a significant association between viral suppression, retention in care, and the use of tuberculosis (TB) prophylaxis among PLHIV. Therefore, TB prophylaxis should be prioritised for all PLHIV without active TB symptoms (Getaneh *et al.*, 2022; Zanoni *et al.*, 2011).

# 6.3.1.4 Behavioural risk factors

Retention in care and viral suppression exhibited significant associations with adherence to ART in the past three days. Programme design should incorporate strategies to enhance adherence. These may include intensive patient education on the importance of ART and the adverse consequences of non-adherence, effective communication between health care providers and PLHIV, involvement of families and caregivers, adherence reminders such as text messages and phone calls, and adherence support programmes.

## 6.3.2 Exploring barriers to viral suppression and retention in care

The retrospective design of this study limited the exploration of barriers to viral suppression and retention in care. To delve into local barriers and gain insight into participants' emotions, opinions, and experiences, qualitative or mixed methods studies that provide a comprehensive understanding and interpret the significance of their actions (Rahman, 2016) could be employed. The findings from such studies can then be integrated into the development of targeted programmes and interventions.

# 6.3.3 COVID pandemic and preparedness

Localized interventions are imperative to mitigate the socioeconomic, psychosocial, and health-related repercussions of the COVID-19 pandemic, thereby contributing to improved retention in care and viral suppression. It is crucial to prioritize the provision of psychosocial and mental health support to address the stigmatization and social isolation experienced by clients during pandemics (Mukamba *et al.*, 2022). Additionally, ensuring an adequate supply of antiretroviral drugs is essential to facilitate the implementation of multi-month scripting and dispensation strategies (Mukamba *et al.*, 2022).



## REFERENCES

Aavani, P. and Allen, L. J. S. (2019) 'The role of CD4 T cells in immune system activation and viral reproduction in a simple model for HIV infection', *Applied Mathematical Modelling*, 75, pp. 210-222. DOI: 10.1016/j.apm.2019.05.028

Abdool Karim, S. S., Churchyard, G. J., Karim, Q. A. and Lawn, S. D. (2009) 'HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response', *Lancet*, 374(9693), pp. 921-33. DOI: 10.1016/S0140-6736(09)60916-8

Abdullahi, S. B., Ibrahim, O. R., Okeji, A. B., Yandoma, R. I., Bashir, I., Haladu, S., Idris, S. A., Oseni, T. I. A., Suleiman, B. M., Yahaya, M., Aworh, M. K. and Sufiyan, M. B. (2021) 'Viral suppression among HIV-positive patients on antiretroviral therapy in northwestern Nigeria: an eleven-year review of tertiary care centre records, January 2009-December 2019', *BMC Infect Dis*, 21(1), pp. 1031. DOI: 10.1186/s12879-021-06722-3

Abdulrahman, S. A., Ganasegeran, K., Rampal, L. and Martins, O. F. (2019) 'HIV Treatment Adherence - A Shared Burden for Patients, Health-Care Providers, and Other Stakeholders', *AIDS Rev*, 21(1), pp. 28-39. DOI: 10.24875/AIDSRev.19000037

Abebe Moges, N., Olubukola, A., Micheal, O. and Berhane, Y. (2020) 'HIV patients retention and attrition in care and their determinants in Ethiopia: a systematic review and meta-analysis', *BMC Infect Dis*, 20(1), pp. 439. DOI: 10.1186/s12879-020-05168-3

Abubakari, A., Issah, H., Mutaka, M. A. O. and Asumah, M. N. (2023) 'Determinants of Virological Failure in HIV Patients on Highly Active Antiretroviral Therapy (HAART): A Retrospective Cross-Sectional Study in the Upper East Region of Ghana', *Venereology*, 2(1), pp. 16-29. DOI: 10.3390/venereology2010002

Adler, N. E. and Newman, K. (2023) 'Socioeconomic disparities in health: pathways and policies ', *Health Aff (Millwood)*, 21(2), pp. 60-76. DOI: 0.1377/hlthaff.21.2.60.

Affenito, S. G., Franko, D. L., Striegel-Moore, R. H. and Thompson, D. (2012) 'Behavioral determinants of obesity: research findings and policy implications', *J Obes*, 2012, pp. 150732. DOI: 10.1155/2012/150732

Altice, F., Evuarherhe, O., Shina, S., Carter, G. and Beaubrun, A. C. (2019) 'Adherence to HIV treatment regimens: systematic literature review and meta-analysis', *Patient Prefer Adherence*, 13, pp. 475-490. DOI: 10.2147/PPA.S192735

Amekudzi, K., Oudraogo, A., Nachega, J. B., Uthman, O. A., Mills, E. J. and Peltzer, K. 2014. The impact of employment on HIV treatment adherence. *In:* Organization, I.L. (ed.). Geneva.

Ammassari, A., Murri, R., Pezzotti, P., Trotta, P. M., Ravasio, L., De Longis, P., Lo Caputo, S., Narciso, P., Pauluzzi, S., Carosi, G., Nappa, S., Piano, P., Izzo, M. C., Lichtner, M., Rezza, G., Monforte, A., Ippolito, G., d'Arminio, M., Wu, W. A. and Antinori, A. (2001) 'Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection', *Journal of acquired immune deficiency syndromes* 28(5), pp. 445-449

Arnsten, J. H., Demas, P. A., Grant, R. W., Gourevitch, M. N., Farzadegan, H., Howard, A. A. and Schoenbaum, E. E. (2002) 'Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users', *J Gen Intern Med.*, 17(5), pp. 377-381. DOI: 10.1046/j.1525-1497.2002.10644.x

Atnafu, A., Haile Mariam, D., Wong, R., Awoke, T. and Wondimeneh, Y. (2015) 'Improving Adult ART Clinic Patient Waiting Time by Implementing an Appointment System at Gondar University Teaching Hospital, Northwest Ethiopia', *Advances in Public Health*, 2015, pp. 1-5. DOI: 10.1155/2015/892464

Avert. (2020). *Tuberculosis and HIV co-infection*. Available: https://www.avert.org/living-with-hiv/health-wellbeing/tuberculosis [Accessed: 03 September 2021].

Ayala, G., Sprague, L., van der Merwe, L. L., Thomas, R. M., Chang, J., Arreola, S., Davis, S. L. M., Taslim, A., Mienies, K., Nilo, A., Mworeko, L., Hikuam, F., de Leon Moreno, C. G. and Izazola-Licea, J. A. (2021) 'Peer- and community-led responses to HIV: A scoping review', *PLoS One*, 16(12), pp. e0260555. DOI: 10.1371/journal.pone.0260555

Ayele, W., Mulugeta, A., Desta, A. and Rabito, F. A. (2015) 'Treatment outcomes and their determinants in HIV patients on Anti-retroviral Treatment Program in selected health facilities of Kembata and Hadiya zones, Southern Nations, Nationalities and Peoples Region, Ethiopia', *BMC Public Health*, 15, pp. 826. DOI: 10.1186/s12889-015-2176-5

Azia, I. N., Mukumbang, F. C. and van Wyk, B. (2016) 'Barriers to adherence to antiretroviral treatment in a regional hospital in Vredenburg, Western Cape, South Africa', *South Afr J HIV Med*, 17(1), pp. 476. DOI: 10.4102/sajhivmed.v17i1.476

Badje, A., Moh, R., Gabillard, D., Guehi, C., Kabran, M., Ntakpe, J. B., Carrou, J. L., Kouame, G. M., Ouattara, E., Messou, E., Anzian, A., Minga, A., Gnokoro, J., Gouesse, P., Emieme, A., Toni, T. D., Rabe, C., Sidibe, B., Nzunetu, G., Dohoun, L., Yao, A., Kamagate, S., Amon, S., Kouame, A. B., Koua, A., Kouame, E., Daligou, M., Hawerlander, D., Ackoundze, S., Koule, S., Seri, J., Ani, A., Dembele, F., Kone, F., Oyebi, M., Mbakop, N., Makaila, O., Babatunde, C., Babatunde, N., Bleoue, G., Tchoutedjem, M., Kouadio, A. C., Sena, G., Yededji, S. Y., Karcher, S., Rouzioux, C., Kouame, A., Assi, R., Bakayoko, A., Domoua, S. K., Deschamps, N., Aka, K., N'Dri-Yoman, T., Salamon, R., Journot, V., Ahibo, H., Ouassa, T., Menan, H., Inwoley, A., Danel, C., Eholie, S. P., Anglaret, X. and Temprano, A. S. G. (2017) 'Effect of isoniazid preventive therapy on risk of death in west African, HIV-infected adults with high CD4 cell counts: long-term follow-up of the Temprano ANRS 12136 trial', *Lancet Glob Health,* 5(11), pp. e1080-e1089. DOI: 10.1016/S2214-109X(17)30372-8

Bangsberg, D. R., Moss, A. R. and Deeks, S. G. (2004) 'Paradoxes of adherence and drug resistance to HIV antiretroviral therapy', *J Antimicrob Chemother*, 53(5), pp. 696-9. DOI: 10.1093/jac/dkh162

Bangsberg, D. R., Perry, S., Charlebois, E. D., Clark, R. A., Roberston, M., Zolopa, A. R. and Moss, A. (2001a) 'Non-adherence to highly active antiretroviral therapy predicts progression to AIDS', *AIDS*, 15(9), pp. 1181-1183

Bangsberg, D. R., Perry, S., Charlebois, E. D., Clark, R. A., Roberston, M., Zolopa, A. R. and Moss, A. (2001b) 'Non-adherence to highly active antiretroviral therapy predicts progression to AIDS', *AIDS*, 15(9), pp. 1181-3. DOI: 10.1097/00002030-200106150-00015

Bangsberg, D. R., Ragland, K., Monk, A. and Deeks, S. G. (2010) 'A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people', *AIDS*, 24(18), pp. 2835-40. DOI: 10.1097/QAD.0b013e328340a209

Barfod, T. S., Sorensen, H. T., Nielsen, H., Rodkjaer, L. and Obel, N. (2006) "Simply forgot' is the most frequently stated reason for missed doses of HAART irrespective of degree of adherence', *HIV Med*, 7(5), pp. 285-90. DOI: 10.1111/j.1468-1293.2006.00387.x

Barnabas, R. V., Revill, P., Tan, N. and Phillips, A. (2017) 'Cost-effectiveness of routine viral load monitoring in low- and middle-income countries: a systematic review', *J Int AIDS Soc*, 20 Suppl 7(Suppl 7). DOI: 10.1002/jia2.25006

Barry, O., Powell, J., Renner, L., Bonney, E. Y., Prin, M., Ampofo, W., Kusah, J., Goka, B., Sagoe, K. W. C., Shabanova, V. and Paintsil, E. (2013) 'Effectiveness of first-line antiretroviral therapy and correlates of longitudinal changes in CD4 and viral load among HIV-

infected children in Ghana.', MC Infectious Diseases, 13(1)

Bastard, M., Fall, M. B. K., Lanièce, I., Taverne, B., Desclaux, A., Ecochard, R., Sow, P. S., Delaporte, E. and Etard, J. F. (2011) 'Revisiting Long-Term Adherence to Highly Active

Antiretroviral Therapy in Senegal Using Latent

Class Analysis', *J Acquir Immune Defic Syndr*, 57(1), pp. 55-61. Available at: <u>https://pubmed.ncbi.nlm.nih.gov/21775934</u>

Bennett, K. K., DeGruttola, V. G., Marschner, I. C., Havlir, D. V. and Richman, D. D. (2002) 'Baseline predictors of CD4 T-lymphocyte recovery with combination antiretroviral therapy', *Journal of Acquired Immune Deficiency Syndromes*, 31(1), pp. 20-26

Berhanu Billoro, B., Mamo, G. and Jarso, H. (2018) 'Adherence to Antiretroviral Therapy and Associated Factors among HIV Infected Patients in Nigist Eleni Mohammed Memorial General Hospital, Hossana, Southern Ethiopia', *Journal of AIDS & Clinical Research*, 09(08). DOI: 10.4172/2155-6113.1000774

Berihun, H., Bazie, G. W., Beyene, A., Zewdie, A. and Kebede, N. (2023) 'Viral suppression and associated factors among children tested for HIV viral load at Amhara Public Health Institute, Dessie Branch, Ethiopia: a cross-sectional study', *BMJ Open*, 13(1), pp. e068792. DOI: 10.1136/bmjopen-2022-068792

Bezabhe, W. M., Chalmers, L., Bereznicki, L. R., Peterson, G. M., Bimirew, M. A. and Kassie, D. M. (2014) 'Barriers and facilitators of adherence to antiretroviral drug therapy and retention

in care among adult HIV-positive patients: a qualitative study from Ethiopia', *PLoS One*, 9(5), pp. e97353. DOI: 10.1371/journal.pone.0097353

Bisson, G. P., Gross, R., Bellamy, S., Chittams, J., Hislop, M., Regensberg, L., Frank, I., Maartens, G. and Nachega, J. B. (2008) 'Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy', *PLoS Med*, 5(5), pp. e109. DOI: 10.1371/journal.pmed.0050109

Bonnet, F., Thiebaut, R., Chene, G., Neau, D., Pellegrin, J. L., Mercie, P., Beylot, J., Dabis, F., Salamon, R., Morlat, P. and Groupe d'Epidemiologie Clinique du, S. e. A. (2005) 'Determinants of clinical progression in antiretroviral-naive HIV-infected patients starting highly active antiretroviral therapy. Aquitaine Cohort, France, 1996-2002', *HIV Med*, 6(3), pp. 198-205. DOI: 10.1111/j.1468-1293.2005.00290.x

Bor, J., Kluberg, S. A., LaValley, M. P., Evans, D., Hirasen, K., Maskew, M., Long, L. and Fox,
M. P. (2022) 'One Pill, Once a Day: Simplified Treatment Regimens and Retention in HIV
Care', *Am J Epidemiol*, 191(6), pp. 999-1008. DOI: 10.1093/aje/kwac006

Boyer, S., Iwuji, C., Gosset, A., Protopopescu, C., Okesola, N., Plazy, M., Spire, B., Orne-Gliemann, J., McGrath, N., Pillay, D., Dabis, F., Larmarange, J. and group, A. T. s. (2016) 'Factors associated with antiretroviral treatment initiation amongst HIV-positive individuals linked to care within a universal test and treat programme: early findings of the ANRS 12249 TasP trial in rural South Africa', *AIDS Care,* 28 Suppl 3(Suppl 3), pp. 39-51. DOI: 10.1080/09540121.2016.1164808

Braithwaite, R. S., Kozal, M. J., Chang, C. C., Roberts, M. S., Fultz, S. L., Goetz, M. B., Gibert, C., Rodriguez-Barradas, M., Mole, L. and Justice, A. C. (2007) 'Adherence, virological and immunological outcomes for HIV-infected veterans starting combination antiretroviral therapies', *AIDS*, 21(12), pp. 1579-89. DOI: 10.1097/QAD.0b013e3281532b31

Brown, J. A., Nsakala, B. L., Mokhele, K., Rakuoane, I., Muhairwe, J., Urda, L., Amstutz, A., Tschumi, N., Klimkait, T. and Labhardt, N. D. (2022) 'Viral suppression after transition from nonnucleoside reverse transcriptase inhibitor- to dolutegravir-based antiretroviral therapy: A prospective cohort study in Lesotho (DO-REAL study)', *HIV Med*, 23(3), pp. 287-293. DOI: 10.1111/hiv.13189

Bulage, L., Ssewanyana, I., Nankabirwa, V., Nsubuga, F., Kihembo, C., Pande, G., Ario, A. R., Matovu, J. K., Wanyenze, R. K. and Kiyaga, C. (2017) 'Factors Associated with Virological Non-suppression among HIV-Positive Patients on Antiretroviral Therapy in Uganda, August 2014-July 2015', *BMC Infect Dis*, 17(1), pp. 326. DOI: 10.1186/s12879-017-2428-3

Buscher, A., Hartman, C., Kallen, M. A. and Giordano, T. P. (2012) 'Impact of antiretroviral dosing frequency and pill burden on adherence among newly diagnosed, antiretroviral-naive HIV patients', *Int J STD AIDS*, 23(5), pp. 351-5. DOI: 10.1258/ijsa.2011.011292

Bussmann, H., Wester, C. W., Ndwapi, N., Grundmann, N., Gaolathe, T., Puvimanasinghe, J., Avalos, A., Mine, M., Seipone, K., Essex, M., Degruttola, V. and Marlink, R. G. (2008) 'Five-year outcomes of initial patients treated in Botswana's National Antiretroviral Treatment Program', *AIDS*, 22(17), pp. 2303-11. DOI: 10.1097/QAD.0b013e3283129db0

Bvochora, T., Satyanarayana, S., Takarinda, K. C., Bara, H., Chonzi, P., Komtenza, B., Duri, C. and Apollo, T. (2019) 'Enhanced adherence counselling and viral load suppression in HIV seropositive patients with an initial high viral load in Harare, Zimbabwe: Operational issues', *PLoS One*, 14(2), pp. e0211326. DOI: 10.1371/journal.pone.0211326

Byrd, K. K., Hou, J. G., Hazen, R., Kirkham, H., Suzuki, S., Clay, P. G., Bush, T., Camp, N. M., Weidle, P. J., Delpino, A. and Patient-Centered, H. I. V. C. M. T. (2019) 'Antiretroviral Adherence Level Necessary for HIV Viral Suppression Using Real-World Data', *J Acquir Immune Defic Syndr*, 82(3), pp. 245-251. DOI: 10.1097/QAI.00000000002142

Campbell, C., Skovdal, M., Madanhire, C., Mugurungi, O., Gregson, S. and Nyamukapa, C. (2011) "We, the AIDS people. . .": how antiretroviral therapy enables Zimbabweans living with HIV/AIDS to cope with stigma', *Am J Public Health*, 101(6), pp. 1004-10. DOI: 10.2105/AJPH.2010.202838

Carvalho, P. P., Barroso, S. M., Coelho, H. C. and Penaforte, F. R. O. (2019) 'Factors associated with antiretroviral therapy adherence in adults: an integrative review of literature', *Cien Saude Colet*, 24(7), pp. 2543-2555. DOI: 10.1590/1413-81232018247.22312017

Chenneville, T., Gabbidon, K., Hanson, P. and Holyfield, C. (2020) 'The Impact of COVID-19 on HIV Treatment and Research: A Call to Action', *Int J Environ Res Public Health*, 17(12). DOI: 10.3390/ijerph17124548

Cherutich, P., Kim, A. A., Kellogg, T. A., Sherr, K., Waruru, A., De Cock, K. M. and Rutherford,
G. W. (2016) 'Detectable HIV Viral Load in Kenya: Data from a Population-Based Survey', *PLoS One*, 11(5), pp. e0154318. DOI: 10.1371/journal.pone.0154318

Chesney, M. A., Ickovics, J. R., Chambers, D. B., Gifford, A. L., Neidig, J., Zwickl, B. and Wu, A. W. (2000) 'Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG)', *AIDS Care*, 12(3), pp. 255-66. DOI: 10.1080/09540120050042891

Clouse, K., Pettifor, A. E., Maskew, M., Bassett, J., Van Rie, A., Behets, F., Gay, C., Sanne, I. and Fox, M. P. (2013) 'Patient retention from HIV diagnosis through one year on antiretroviral therapy at a primary health care clinic in Johannesburg, South Africa', *J Acquir Immune Defic Syndr*, 62(2), pp. e39-46. DOI: 10.1097/QAI.0b013e318273ac48

Cohen, C. J., Meyers, J. L. and Davis, K. L. (2013) 'Association between daily antiretroviral pill burden and treatment adherence, hospitalisation risk, and other healthcare utilisation and costs in a US medicaid population with HIV', *BMJ Open*, 3(8). DOI: 10.1136/bmjopen-2013-003028

Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., Hakim, J. G., Kumwenda, J., Grinsztejn, B., Pilotto, J. H., Godbole, S. V., Mehendale, S., Chariyalertsak, S., Santos, B. R., Mayer, K. H., Hoffman, I. F., Eshleman, S. H., Piwowar-Manning, E., Wang, L., Makhema, J., Mills, L. A., de Bruyn, G., Sanne, I., Eron, J., Gallant, J., Havlir, D., Swindells, S., Ribaudo, H., Elharrar, V., Burns, D., Taha, T. E., Nielsen-Saines, K., Celentano, D., Essex, M., Fleming, T. R. and Team, H. S. (2011) 'Prevention of HIV-1 infection with early antiretroviral therapy', *N Engl J Med*, 365(6), pp. 493-505. DOI: 10.1056/NEJMoa1105243

Cooke, G. S., Tanser, F. C., Barnighausen, T. W. and Newell, M. L. (2010) 'Population uptake of antiretroviral treatment through primary care in rural South Africa', *BMC Public Health*, 10, pp. 585. DOI: 10.1186/1471-2458-10-585

Cornell, M., Schomaker, M., Garone, D. B., Giddy, J., Hoffmann, C. J., Lessells, R., Maskew, M., Prozesky, H., Wood, R., Johnson, L. F., Egger, M., Boulle, A., Myer, L. and International Epidemiologic Databases to Evaluate, A. S. A. C. (2012) 'Gender differences in survival among

adult patients starting antiretroviral therapy in South Africa: a multicentre cohort study', *PLoS Med*, 9(9), pp. e1001304. DOI: 10.1371/journal.pmed.1001304

Cucinotta, D. and Vanelli, M. (2020) 'WHO Declares COVID-19 a Pandemic', *Acta Biomed*, 91(1), pp. 157-160. DOI: 10.23750/abm.v91i1.9397

Dan-Jumbo, A. and Okuku, M. O. (2021) 'Adverse Drug Effects and Non-Adherence to Antiretroviral Therapy in Nigeria: A Review', *Asian Journal of Advanced Research and Reports*, pp. 19-25. DOI: 10.9734/ajarr/2021/v15i130354

Dansereau, E., Masiye, F., Gakidou, E., Masters, S. H., Burstein, R. and Kumar, S. (2015) 'Patient satisfaction and perceived quality of care: evidence from a cross-sectional national exit survey of HIV and non-HIV service users in Zambia', *BMJ Open*, 5(12), pp. e009700. DOI: 10.1136/bmjopen-2015-009700

de Fatima Bonolo, P., Ceccato, M., Rocha, G. M., de Assis Acurcio, F., Campos, L. N. and Guimaraes, M. D. (2013) 'Gender differences in non-adherence among Brazilian patients initiating antiretroviral therapy', *Clinics (Sao Paulo)*, 68(5), pp. 612-20. DOI: 10.6061/clinics/2013(05)06

Dessie, G., Wagnew, F., Mulugeta, H., Amare, D., Jara, D., Leshargie, C. T., Negesse, A., Rayasam, S. and Burrowes, S. (2019) 'The effect of disclosure on adherence to antiretroviral therapy among adults living with HIV in Ethiopia: a systematic review and meta-analysis', *BMC Infect Dis*, 19(1), pp. 528. DOI: 10.1186/s12879-019-4148-3

Desta, A. A., Woldearegay, T. W., Futwi, N., Gebrehiwot, G. T., Gebru, G. G., Berhe, A. A. and Godefay, H. (2020) 'HIV virological non-suppression and factors associated with non-suppression among adolescents and adults on antiretroviral therapy in northern Ethiopia: a retrospective study', *BMC Infect Dis*, 20(1), pp. 4. DOI: 10.1186/s12879-019-4732-6

Detels, R., Munoz, A., McFarlane, G., Kingsley, L. A., Margolick, J. B., Giorgi, J., Schrager, L. K. and Phair, J. P. (1998) 'Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. Multicenter AIDS Cohort Study Investigators', *JAMA*, 280(17), pp. 1497-503. DOI: 10.1001/jama.280.17.1497

Devnani, M., Gupta, A. K., Wanchu, A. and Sharma, R. K. (2012) 'Factors associated with health service satisfaction among people living with HIV/AIDS: a cross sectional study at ART

center in Chandigarh, India', *AIDS Care*, 24(1), pp. 100-7. DOI: 10.1080/09540121.2011.592816

Di Carlo, D., Falasca, F., Palermo, E., Mezzaroma, I., Fimiani, C., Siccardi, G., Celani, L., Di Campli, F. M., d'Ettorre, G., Antonelli, G. and Turriziani, O. (2021) 'Dolutegravir-Based Regimen for Maintenance of Viral Suppression in People Living with HIV: 48-Week Results in Real-Life Setting', *AIDS Res Hum Retroviruses*, 37(6), pp. 478-485. DOI: 10.1089/AID.2020.0196

Dorcelus, L., Bernard, J., Jr., Georgery, C. and Vanessa, C. (2021) 'Factors associated with antiretroviral therapy adherence among people living with HIV in Haiti: a cross-sectional study', *AIDS Res Ther*, 18(1), pp. 81. DOI: 10.1186/s12981-021-00405-4

Dowshen, N. and D'Angelo, L. (2011) 'Health care transition for youth living with HIV/AIDS', *Pediatrics*, 128(4), pp. 762-71. DOI: 10.1542/peds.2011-0068

Drain, P. K. and Garrett, N. (2020) 'SARS-CoV-2 pandemic expanding in sub-Saharan Africa: Considerations for COVID-19 in people living with HIV', *EClinicalMedicine*, 22, pp. 100342. DOI: 10.1016/j.eclinm.2020.100342

Dye, C., Harries, A. D., Maher, D., Hosseini, S. M., Nkhoma, W. and Salaniponi, F. M. (2006) 'Tuberculosis', in Jamison, D.T., Feachem, R.G., Makgoba, M.W., Bos, E.R., Baingana, F.K., Hofman, K.J. and Rogo, K.O. (eds.) *Disease and Mortality in Sub-Saharan Africa*. 2nd ed. Washington (DC).

Dyer, J., Wilson, K., Badia, J., Agot, K., Neary, J., Njuguna, I., Kibugi, J., Healy, E., Beima-Sofie, K., John-Stewart, G. and Kohler, P. (2021) 'The Psychosocial Effects of the COVID-19 Pandemic on Youth Living with HIV in Western Kenya', *AIDS Behav*, 25(1), pp. 68-72. DOI: 10.1007/s10461-020-03005-x

Eduardo, E., Lamb, M. R., Kandula, S., Howard, A., Mugisha, V., Kimanga, D., Kilama, B., El-Sadr, W. and Elul, B. (2014) 'Characteristics and outcomes among older HIV-positive adults enrolled in HIV programs in four sub-Saharan African countries', *PLoS One*, 9(7), pp. e103864. DOI: 10.1371/journal.pone.0103864

Elul, B., Basinga, P., Nuwagaba-Biribonwoha, H., Saito, S., Horowitz, D., Nash, D., Mugabo, J., Mugisha, V., Rugigana, E., Nkunda, R. and Asiimwe, A. (2013) 'High levels of adherence

and viral suppression in a nationally representative sample of HIV-infected adults on antiretroviral therapy for 6, 12 and 18 months in Rwanda', *PLoS One*, 8(1), pp. e53586. DOI: 10.1371/journal.pone.0053586

Esber, A., Dear, N., Shah, N., Kibuuka, H., Maswai, J., Owuoth, J., Singoei, V., Bahemana, E., Iroezindu, M., Crowell, T. A., Polyak, C. S., Cavanaugh, J. S., Ake, J. A. and Group, A. S. (2022) 'Brief Report: Virologic Impact of the Dolutegravir Transition: Prospective Results From the Multinational African Cohort Study', *J Acquir Immune Defic Syndr*, 91(3), pp. 285-289. DOI: 10.1097/QAI.00000000003065

Fatti, G., Mothibi, E., Meintjes, G. and Grimwood, A. (2014) 'Antiretroviral treatment outcomes amongst older adults in a large multicentre cohort in South Africa', *PLoS One*, 9(6), pp. e100273. DOI: 10.1371/journal.pone.0100273

Filimao, D. B. C., Moon, T. D., Senise, J. F., Diaz, R. S., Sidat, M. and Castelo, A. (2019) 'Individual factors associated with time to non-adherence to ART pick-up within HIV care and treatment services in three health facilities of Zambezia Province, Mozambique', *PLoS One*, 14(3), pp. e0213804. DOI: 10.1371/journal.pone.0213804

Flynn, P. M., Rudy, B. J., Douglas, S. D., Lathey, J., Spector, S. A., Martinez, J., Silio, M., Belzer, M., Friedman, L., D'Angelo, L., McNamara, J., Hodge, J., Hughes, M. D., Lindsey, J. C. and Pediatric, A. C. T. G. S. T. (2004) 'Virologic and immunologic outcomes after 24 weeks in HIV type 1-infected adolescents receiving highly active antiretroviral therapy', *J Infect Dis*, 190(2), pp. 271-9. DOI: 10.1086/421521

Fokam, J., Sosso, S. M., Yagai, B., Billong, S. C., Djubgang Mbadie, R. E., Kamgaing Simo, R., Edimo, S. V., Nka, A. D., Tiga Ayissi, A., Yimga, J. F., Takou, D., Moudourou, S., Ngo Nemb, M., Nfetam Elat, J. B., Santoro, M. M., Perno, C. F., Colizzi, V. and Ndjolo, A. (2019) 'Viral suppression in adults, adolescents and children receiving antiretroviral therapy in Cameroon: adolescents at high risk of virological failure in the era of "test and treat", *AIDS Res Ther*, 16(1), pp. 36. DOI: 10.1186/s12981-019-0252-0

Fox, M. P. and Rosen, S. (2010) 'Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007-2009: systematic review', *Trop Med Int Health*, 15 Suppl 1(s1), pp. 1-15. DOI: 10.1111/j.1365-3156.2010.02508.x

Frescura, L., Godfrey-Faussett, P., Feizzadeh, A. A., El-Sadr, W., Syarif, O., Ghys, P. D., on and behalf of the testing treatment target Working, G. (2022) 'Achieving the 95 95 95 targets for all: A pathway to ending AIDS', *PLoS One*, 17(8), pp. e0272405. DOI: 10.1371/journal.pone.0272405

Gaolathe, T., Wirth, K. E., Holme, M. P., Makhema, J., Moyo, S., Chakalisa, U., Yankinda, E. K., Lei, Q., Mmalane, M., Novitsky, V., Okui, L., van Widenfelt, E., Powis, K. M., Khan, N., Bennett, K., Bussmann, H., Dryden-Peterson, S., Lebelonyane, R., El-Halabi, S., Mills, L. A., Marukutira, T., Wang, R., Tchetgen, E. J., DeGruttola, V., Essex, M., Lockman, S. and Botswana Combination Prevention Project study, t. (2016) 'Botswana's progress toward achieving the 2020 UNAIDS 90-90-90 antiretroviral therapy and virological suppression goals: a population-based survey', *Lancet HIV*, 3(5), pp. e221-30. DOI: 10.1016/S2352-3018(16)00037-0

Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C. and Burman, W. J. (2011) 'The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection', *Clin Infect Dis*, 52(6), pp. 793-800. DOI: 10.1093/cid/ciq243

Geng, E. H., Bangsberg, D. R., Musinguzi, N., Emenyonu, N., Bwana, M. B., Yiannoutsos, C. T., Glidden, D. V., Deeks, S. G. and Martin, J. N. (2010a) 'Understanding reasons for and outcomes of patients lost to follow-up in antiretroviral therapy programs in Africa through a sampling-based approach', *J Acquir Immune Defic Syndr*; 53(3), pp. 405-11. DOI: 10.1097/QAI.0b013e3181b843f0

Geng, E. H., Nash, D., Kambugu, A., Zhang, Y., Braitstein, P., Christopoulos, K. A., Muyindike, W., Bwana, M. B., Yiannoutsos, C. T., Petersen, M. L. and Martin, J. N. (2010b) 'Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions', *Curr HIV/AIDS Rep*, 7(4), pp. 234-44. DOI: 10.1007/s11904-010-0061-5

Getaneh, T., Negesse, A., Dessie, G. and Desta, M. (2022) 'The impact of tuberculosis coinfection on virological failure among adults living with HIV in Ethiopia: A systematic review and meta-analysis', *J Clin Tuberc Other Mycobact Dis*, 27, pp. 100310. DOI: 10.1016/j.jctube.2022.100310

Ghidei, L., Simone, M. J., Salow, M. J., Zimmerman, K. M., Paquin, A. M., Skarf, L. M., Kostas, T. R. and Rudolph, J. L. (2013) 'Aging, antiretrovirals, and adherence: a meta analysis

of adherence among older HIV-infected individuals', *Drugs Aging*, 30(10), pp. 809-19. DOI: 10.1007/s40266-013-0107-7

Giordano, T. P., Gifford, A. L., White, A. C., Jr., Suarez-Almazor, M. E., Rabeneck, L., Hartman, C., Backus, L. I., Mole, L. A. and Morgan, R. O. (2007) 'Retention in care: a challenge to survival with HIV infection', *Clin Infect Dis*, 44(11), pp. 1493-9. DOI: 10.1086/516778

Glass, T. and Cavassini, M. (2014) 'Asking about adherence - from flipping the coin to strong evidence', *Swiss Med Wkly*, 144, pp. w14016. DOI: 10.4414/smw.2014.14016

Glass, T., Myer, L. and Lesosky, M. (2020) 'The role of HIV viral load in mathematical models of HIV transmission and treatment: a review', *BMJ Glob Health*, 5(1), pp. e001800. DOI: 10.1136/bmjgh-2019-001800

Goletti, D., Weissman, D., Jackson, R. W., Graham, N. M., Vlahov, D., Klein, R. S., Munsiff, S. S., Ortona, L., Cauda, R. and Fauci, A. S. (1996) 'Effect of Mycobacterium tuberculosis on HIV replication. Role of immune activation', *J Immunol*, 157(3), pp. 1271-8. Available at: <u>https://www.ncbi.nlm.nih.gov/pubmed/8757635</u>

Grabar, S., Le Moing, V., Goujard, C., Egger, M., Leport, C., Kazatchkine, M. D., Weiss, L. and Costagliola, D. (2005) 'Response to highly active antiretroviral therapy at 6 months and long-term disease progression in HIV-1 infection', *J Acquir Immune Defic Syndr*, 39(3), pp. 284-92. DOI: 10.1097/01.qai.0000160925.33935.72

Graham, S. M., Mugo, P., Gichuru, E., Thiong'o, A., Macharia, M., Okuku, H. S., van der Elst, E., Price, M. A., Muraguri, N. and Sanders, E. J. (2013) 'Adherence to antiretroviral therapy and clinical outcomes among young adults reporting high-risk sexual behavior, including men who have sex with men, in coastal Kenya', *AIDS Behav*, 17(4), pp. 1255-65. DOI: 10.1007/s10461-013-0445-9

Green, D., Tordoff, D. M., Kharono, B., Akullian, A., Bershteyn, A., Morrison, M., Garnett, G., Duerr, A. and Drain, P. K. (2020) 'Evidence of sociodemographic heterogeneity across the HIV treatment cascade and progress towards 90-90-90 in sub-Saharan Africa - a systematic review and meta-analysis', *J Int AIDS Soc*, 23(3), pp. e25470. DOI: 10.1002/jia2.25470

Grimes, D. E., Andrade, R. A., Niemeyer, C. R. and Grimes, R. M. (2013) 'Measurement issues in using pharmacy records to calculate adherence to antiretroviral drugs', *HIV Clin Trials*, 14(2), pp. 68-74. DOI: 10.1310/hct1402-68

Grobler, A., Cawood, C., Khanyile, D., Puren, A. and Kharsany, A. B. M. (2017) 'Progress of UNAIDS 90-90-90 targets in a district in KwaZulu-Natal, South Africa, with high HIV burden, in the HIPSS study: a household-based complex multilevel community survey', *Lancet HIV*, 4(11), pp. e505-e513. DOI: 10.1016/S2352-3018(17)30122-4

Gumede, S. B., Venter, F., de Wit, J., Wensing, A. and Lalla-Edward, S. T. (2022) 'Antiretroviral therapy uptake and predictors of virological failure in patients with HIV receiving first-line and second-line regimens in Johannesburg, South Africa: a retrospective cohort data analysis', *BMJ Open*, 12(4), pp. e054019. DOI: 10.1136/bmjopen-2021-054019

Gunda, D. W., Kilonzo, S. B., Bulegesi, S. M., Mpondo, B. C. T. and Shao, E. R. (2016) 'Risk factors for mortality among tuberculosis patients on treatment at Bugando Medical Centre in north-western Tanzania: a retrospective cross-sectional study', *Tanzania Journal of Health Research*, 18(4). DOI: 10.4314/thrb.v18i4.1

Haghighat, R., Toska, E., Bungane, N. and Cluver, L. (2021) 'The HIV care cascade for adolescents initiated on antiretroviral therapy in a health district of South Africa: a retrospective cohort study', *BMC Infect Dis*, 21(1), pp. 60. DOI: 10.1186/s12879-020-05742-9

Haider, M. R., Brown, M. J., Harrison, S., Yang, X., Ingram, L., Bhochhibhoya, A., Hamilton, A., Olatosi, B. and Li, X. (2021) 'Sociodemographic factors affecting viral load suppression among people living with HIV in South Carolina', *AIDS Care*, 33(3), pp. 290-298. DOI: 10.1080/09540121.2019.1703892

Hamada, Y., Getahun, H., Tadesse, B. T. and Ford, N. (2021) 'HIV-associated tuberculosis', *Int J STD AIDS*, 32(9), pp. 780-790. DOI: 10.1177/0956462421992257

Harzke, A. J., Williams, M. L., Nilsson-Schonnesson, L., Ross, M. W., Timpson, S. and Keel, K. B. (2004) 'Psychosocial factors associated with adherence to antiretroviral medications in a sample of HIV-positive African American drug users', *AIDS Care*, 16(4), pp. 458-70. DOI: 10.1080/09540120410001683394

Hendershot, C. S., Stoner, S. A., Pantalone, D. W. and Simoni, J. M. (2009) 'Alcohol use and antiretroviral adherence: review and meta-analysis', *J Acquir Immune Defic Syndr*, 52(2), pp. 180-202. DOI: 10.1097/QAI.0b013e3181b18b6e

Hirasen, K., Fox, M. P., Hendrickson, C. J., Sineke, T. and Onoya, D. (2020) 'HIV Treatment Outcomes Among Patients Initiated on Antiretroviral Therapy Pre and Post-Universal Test and Treat Guidelines in South Africa', *Ther Clin Risk Manag*, 16, pp. 169-180. DOI: 10.2147/TCRM.S227290

Hiregoudar, V., Bellara, R. and Goud, T. G. (2019) 'Proportion and Determinants of Adherence to Antiretroviral Therapy among HIV Positive People Registered Under ART Center in South India', *Int J Prev Med*, 10, pp. 206. DOI: 10.4103/ijpvm.IJPVM\_7\_18

Hogan, A. B., Jewell, B. L., Sherrard-Smith, E., Vesga, J. F., Watson, O. J., Whittaker, C.,
Hamlet, A., Smith, J. A., Winskill, P., Verity, R., Baguelin, M., Lees, J. A., Whittles, L. K.,
Ainslie, K. E. C., Bhatt, S., Boonyasiri, A., Brazeau, N. F., Cattarino, L., Cooper, L. V.,
Coupland, H., Cuomo-Dannenburg, G., Dighe, A., Djaafara, B. A., Donnelly, C. A., Eaton, J.
W., van Elsland, S. L., FitzJohn, R. G., Fu, H., Gaythorpe, K. A. M., Green, W., Haw, D. J.,
Hayes, S., Hinsley, W., Imai, N., Laydon, D. J., Mangal, T. D., Mellan, T. A., Mishra, S.,
Nedjati-Gilani, G., Parag, K. V., Thompson, H. A., Unwin, H. J. T., Vollmer, M. A. C., Walters,
C. E., Wang, H., Wang, Y., Xi, X., Ferguson, N. M., Okell, L. C., Churcher, T. S.,
Arinaminpathy, N., Ghani, A. C., Walker, P. G. T. and Hallett, T. B. (2020) 'Potential impact of
the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income
countries: a modelling study', *Lancet Glob Health*, 8(9), pp. e1132-e1141. DOI:
10.1016/S2214-109X(20)30288-6

Holmes, C. B., Sikazwe, I., Sikombe, K., Eshun-Wilson, I., Czaicki, N., Beres, L. K., Mukamba, N., Simbeza, S., Bolton Moore, C., Hantuba, C., Mwaba, P., Phiri, C., Padian, N., Glidden, D. V. and Geng, E. (2018) 'Estimated mortality on HIV treatment among active patients and patients lost to follow-up in 4 provinces of Zambia: Findings from a multistage sampling-based survey', *PLoS Med*, 15(1), pp. e1002489. DOI: 10.1371/journal.pmed.1002489

Howard, A. A., Arnsten, J. H., Lo, Y., Vlahov, D., Rich, J. D., Schuman, P., Stone, V. E., Smith, D. K., Schoenbaum, E. E. and Group, H. E. R. S. (2002) 'A prospective study of adherence and viral load in a large multi-center cohort of HIV-infected women', *AIDS*, 16(16), pp. 2175-82. DOI: 10.1097/00002030-200211080-00010

Human Sciences Research Council. (2017). Fifth South African National HIV prevalence, incidence, behaviour and communication survey.

Iacob, S. A., Iacob, D. G. and Jugulete, G. (2017) 'Improving the Adherence to Antiretroviral Therapy, a Difficult but Essential Task for a Successful HIV Treatment-Clinical Points of View and Practical Considerations', *Front Pharmacol*, 8, pp. 831. DOI: 10.3389/fphar.2017.00831

Isaac, E. W., Ajani, A., Difa, A. J., Aremu, J. T., Oluwaseun, O. C. and Hassan, M. D. (2021) 'Viral Suppression in Adult Nigerians in a Regional Antiretroviral Therapy Programme: A Cross Sectional Descriptive Study', *World Journal of AIDS*, 11(01), pp. 1-14. DOI: 10.4236/wja.2021.111001

Izudi, J., Mugenyi, J., Mugabekazi, M., Muwanika, B., Tumukunde Spector, V., Katawera, A. and Kekitiinwa, A. (2018) 'Retention of HIV-Positive Adolescents in Care: A Quality Improvement Intervention in Mid-Western Uganda', *Biomed Res Int*, 2018, pp. 1524016. DOI: 10.1155/2018/1524016

Jain, V., Byonanebye, D. M., Amanyire, G., Kwarisiima, D., Black, D., Kabami, J., Chamie, G., Clark, T. D., Rooney, J. F., Charlebois, E. D., Kamya, M. R., Havlir, D. V. and Collaboration, S. (2014) 'Successful antiretroviral therapy delivery and retention in care among asymptomatic individuals with high CD4+ T-cell counts above 350 cells/mul in rural Uganda', *AIDS*, 28(15), pp. 2241-9. DOI: 10.1097/QAD.0000000000000001

Jalal, T. M. T., Abdullah, S., Wahab, F. A., Dir, S. and Naing, N. N. (2017) 'Prevalence and Factors Associated with Tuberculosis Treatment Success among TB/HIV Co-Infection in North-East Malaysia', *Malays J Med Sci*, 24(6), pp. 75-82. DOI: 10.21315/mjms2017.24.6.9

Jiang, H., Zhou, Y. and Tang, W. (2020) 'Maintaining HIV care during the COVID-19 pandemic', *Lancet HIV*, 7(5), pp. e308-e309. DOI: 10.1016/S2352-3018(20)30105-3

Jo, Y., Rosen, S., Sy, K. T. L., Phiri, B., Huber, A. N., Mwansa, M., Shakwelele, H., Haimbe, P., Mwenechanya, M. M., Lumano-Mulenga, P. and Nichols, B. E. (2021) 'Changes in HIV treatment differentiated care uptake during the COVID-19 pandemic in Zambia: interrupted time series analysis', *J Int AIDS Soc*, 24 Suppl 6(Suppl 6), pp. e25808. DOI: 10.1002/jia2.25808

Jobanputra, K., Parker, L. A., Azih, C., Okello, V., Maphalala, G., Kershberger, B., Khogali, M., Lujan, J., Antierens, A., Teck, R., Ellman, T., Kosgei, R. and Reid, T. (2015) 'Factors

associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland', *PLoS One*, 10(2), pp. e0116144. DOI: 10.1371/journal.pone.0116144

Johnson, M. O., Dilworth, S. E., Taylor, J. M. and Neilands, T. B. (2011) 'Improving coping skills for self-management of treatment side effects can reduce antiretroviral medication nonadherence among people living with HIV', *Ann Behav Med*, 41(1), pp. 83-91. DOI: 10.1007/s12160-010-9230-4

Joseph Afe, A., Motunrayo, O. and Ogungbade, G. (2018) 'Factors Influencing Adherence to HAART among Patients Living with HIV Infection in Southwest Nigeria: A Cross-Sectional Analysis', *Journal of HIV & Retro Virus*, 04(01). DOI: 10.21767/2471-9676.100033

Joseph, B., Kerr, T., Puskas, C. M., Montaner, J., Wood, E. and Milloy, M. J. (2015) 'Factors linked to transitions in adherence to antiretroviral therapy among HIV-infected illicit drug users in a Canadian setting', *AIDS Care*, 27(9), pp. 1128-36. DOI: 10.1080/09540121.2015.1032205

Joseph Davey, D., Abrahams, Z., Feinberg, M., Prins, M., Serrao, C., Medeossi, B. and Darkoh, E. (2018) 'Factors associated with recent unsuppressed viral load in HIV-1-infected patients in care on first-line antiretroviral therapy in South Africa', *Int J STD AIDS*, 29(6), pp. 603-610. DOI: 10.1177/0956462417748859

Kafwanka, P., Nalule, F. M. and Michelo, C. (2023) 'Poor adherence to antiretroviral therapy among adult people living with HIV initiated during the COVID-19 epidemic waves - observations at the University Teaching Hospital in Lusaka, Zambia', *Front Public Health*, 11, pp. 1094214. DOI: 10.3389/fpubh.2023.1094214

Kaira, M., Sikazwe, T., Simwanza, J., Zambwe, M. and Chipimo, P. J. (2021) 'Evaluating the Outcomes of Enhanced Adherence Counselling Intervention on Clients with High Viral Loads in Selected Health Facilities in Monze District', *BMJ*, pp. 1-18. DOI: 10.1101/2021.12.18.21267844

Kakkar, F., Van der Linden, D., Valois, S., Maurice, F., Onnorouille, M., Lapointe, N., Soudeyns, H. and Lamarre, V. (2016) 'Health outcomes and the transition experience of HIV-infected adolescents after transfer to adult care in Quebec, Canada', *BMC Pediatr*, 16, pp. 109. DOI: 10.1186/s12887-016-0644-4

Kalichman, S. C., Amaral, C. M., White, D., Swetsze, C., Pope, H., Kalichman, M. O., Cherry, C. and Eaton, L. (2009) 'Prevalence and clinical implications of interactive toxicity beliefs regarding mixing alcohol and antiretroviral therapies among people living with HIV/AIDS', *AIDS Patient Care STDS*, 23(6), pp. 449-54. DOI: 10.1089/apc.2008.0184

Kiplagat, J., Mwangi, A., Keter, A., Braitstein, P., Sang, E., Negin, J. and Chasela, C. (2018) 'Retention in care among older adults living with HIV in western Kenya: A retrospective observational cohort study', *PLoS One*, 13(3), pp. e0194047. DOI: 10.1371/journal.pone.0194047

Kiwanuka, J., Mukulu Waila, J., Muhindo Kahungu, M., Kitonsa, J. and Kiwanuka, N. (2020) 'Determinants of loss to follow-up among HIV positive patients receiving antiretroviral therapy in a test and treat setting: A retrospective cohort study in Masaka, Uganda', *PLoS One*, 15(4), pp. e0217606. DOI: 10.1371/journal.pone.0217606

Knodel, J., Kespichayawattana, J., Saengtienchai, C. and Wiwatwanich, S. (2010) 'The role of parents and family members in ART treatment adherence: Evidence from Thailand', *Res Aging*, 32(1), pp. 19-39. DOI: 10.1177/0164027509348130

Kunutsor, S., Walley, J., Katabira, E., Muchuro, S., Balidawa, H., Namagala, E. and Ikoona, E. (2010) 'Clinic Attendance for Medication Refills and Medication Adherence amongst an Antiretroviral Treatment Cohort in Uganda: A Prospective Study', *AIDS Res Treat*, 2010, pp. 872396. DOI: 10.1155/2010/872396

Lamb, M. R., Fayorsey, R., Nuwagaba-Biribonwoha, H., Viola, V., Mutabazi, V., Alwar, T., Casalini, C. and Elul, B. (2014) 'High attrition before and after ART initiation among youth (15-24 years of age) enrolled in HIV care', *AIDS*, 28(4), pp. 559-68. DOI: 10.1097/QAD.000000000000054

Lankowski, A. J., Siedner, M. J., Bangsberg, D. R. and Tsai, A. C. (2014) 'Impact of geographic and transportation-related barriers on HIV outcomes in sub-Saharan Africa: a systematic review', *AIDS Behav*, 18(7), pp. 1199-223. DOI: 10.1007/s10461-014-0729-8

Lee, W. K., Milloy, M. J. S., Nosova, E., Walsh, J. and Kerr, T. (2019) 'Predictors of Antiretroviral Adherence Self-efficacy Among People Living With HIV/AIDS in a Canadian

Setting', *J Acquir Immune Defic Syndr*, 80(1), pp. 103-109. DOI: 10.1097/QAI.00000000001878

Liu, H., Golin, C. E., Miller, L. G., Hays, R. D., Beck, C. K., Sanandaji, S., Christian, J., Maldonado, T., Duran, D., Kaplan, A. H. and Wenger, N. S. (2001) 'A comparison study of multiple measures of adherence to HIV protease inhibitors', *Ann Intern Med*, 134(10), pp. 968-77. DOI: 10.7326/0003-4819-134-10-200105150-00011

Lokpo, S. Y., Ofori-Attah, P. J., Ameke, L. S., Obirikorang, C., Orish, V. N., Kpene, G. E., Agboli, E., Kye-Duodu, G., Deku, J. G., Awadzi, B. K., Noagbe, M. and Tetteh Quarshie, S. (2020) 'Viral Suppression and Its Associated Factors in HIV Patients on Highly Active Antiretroviral Therapy (HAART): A Retrospective Study in the Ho Municipality, Ghana', *AIDS Research and Treatment*, 2020, pp. 1-7. DOI: 10.1155/2020/9247451

Loutfy, M. R., Wu, W., Letchumanan, M., Bondy, L., Antoniou, T., Margolese, S., Zhang, Y., Rueda, S., McGee, F., Peck, R., Binder, L., Allard, P., Rourke, S. B. and Rochon, P. A. (2013) 'Systematic review of HIV transmission between heterosexual serodiscordant couples where the HIV-positive partner is fully suppressed on antiretroviral therapy', *PLoS One*, 8(2), pp. e55747. DOI: 10.1371/journal.pone.0055747

Mahomed, H. and Bachmann, O. M. (1998) 'Block appointments in an overloaded South African health centre Quantitative and qualitative evaluation', *International Journal of Health Care Quality Assurance*, 11(4-5), pp. 123-126. DOI: 10.1108/09526869810216043

Malamba, S. S., Morgan, D., Clayton, T., Mayanja, B., Okongo, M. and Whitworth, J. (1999) 'The prognostic value of the World Health Organisation staging system for HIV infection and disease in rural Uganda', *AIDS*, 13(18), pp. 2555-62. DOI: 10.1097/00002030-199912240-00009

Mannheimer, S. B., Matts, J., Telzak, E., Chesney, M., Child, C., Wu, A. W., Friedland, G. and Terry Beirn Community Programs for Clinical Research on, A. (2005) 'Quality of life in HIVinfected individuals receiving antiretroviral therapy is related to adherence', *AIDS Care*, 17(1), pp. 10-22. DOI: 10.1080/09540120412331305098 Marcellin, F., Spire, B., Patrizia, M. and Roux, P. C. (2013) 'Assessing adherence to antiretroviral therapy in randomized HIV clinical trials: a review of currently used methods', *Expert Rev Anti Infect Ther*, 11(3), pp. 239-250. DOI: 10.1586/eri.13.8.

Martinez-Mesa, J., Gonzalez-Chica, D. A., Duquia, R. P., Bonamigo, R. R. and Bastos, J. L. (2016) 'Sampling: how to select participants in my research study?', *An Bras Dermatol*, 91(3), pp. 326-30. DOI: 10.1590/abd1806-4841.20165254

Martos-Méndez, M. J. (2015) 'Self-efficacy adn adherence to treatment: The mediating effects of social support', *Journal of Behavior, Health & Social Issues,* 7(2), pp. 19-29. DOI: 10.5460/jbhsi.v7.2.52889

Massaquoi, M., Zachariah, R., Manzi, M., Pasulani, O., Misindi, D., Mwagomba, B., Bauernfeind, A. and Harries, A. D. (2009) 'Patient retention and attrition on antiretroviral treatment at district level in rural Malawi', *Trans R Soc Trop Med Hyg*, 103(6), pp. 594-600. DOI: 10.1016/j.trstmh.2009.02.012

Mbuagbaw, L., Thabane, L., Ongolo-Zogo, P., Yondo, D., Noorduyn, S., Smieja, M. and Dolovich, L. (2012) 'Trends and determining factors associated with adherence to antiretroviral therapy (ART) in Cameroon: a systematic review and analysis of the CAMPS trial', *AIDS Res Ther*, 9(1), pp. 37. DOI: 10.1186/1742-6405-9-37

Mehari, E. A., Muche, E. A. and Gonete, K. A. (2021) 'Virological Suppression and Its Associated Factors of Dolutegravir Based Regimen in a Resource-Limited Setting: An Observational Retrospective Study in Ethiopia', *HIV AIDS (Auckl)*, 13, pp. 709-717. DOI: 10.2147/HIV.S316776

Melgar, M., Nichols, C., Cavanaugh, J. S., Kirking, H. L., Surie, D., Date, A., Ahmedov, S., Maloney, S., Fukunaga, R., Advisors, C. D. C. O. T. H., National, M. and Departments of Health Tuberculosis Program, M. (2020) 'Tuberculosis Preventive Treatment Scale-Up Among Antiretroviral Therapy Patients - 16 Countries Supported by the U.S. President's Emergency Plan for AIDS Relief, 2017-2019', *MMWR Morb Mortal Wkly Rep*, 69(12), pp. 329-334. DOI: 10.15585/mmwr.mm6912a3

Meloni, S. T., Chang, C. A., Eisen, G., Jolayemi, T., Banigbe, B., Okonkwo, P. I. and Kanki, P. J. (2016) 'Long-Term Outcomes on Antiretroviral Therapy in a Large Scale-Up Program in Nigeria', *PLoS One*, 11(10), pp. e0164030. DOI: 10.1371/journal.pone.0164030

Mocroft, A., Madge, S., Johnson, A. M., Lazzarin, A., Clumeck, N., Goebel, F. D., Viard, J. P., Gatell, J., Blaxhult, A. and Lundgren, J. D. (1999) 'A comparison of exposure groups in the EuroSIDA study: starting highly active antiretroviral therapy (HAART), response to HAART, and survival', *J Acquir Immune Defic Syndr*, 22(4), pp. 369-78. DOI: 10.1097/00126334-199912010-00008

Mogosetsi, N. J., Mabuza, L. H. and Ogunbanjo, G. A. (2018) 'The Prevalence of HIV Load Suppression and Related Factors Among Patients on ART at Phedisong 4 Clinic, Pretoria, South Africa', *The Open Public Health Journal*, 11(1), pp. 135-146. DOI: 10.2174/1874944501811010135

MOH (2014) Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection, Lusaka: Ministry of Health.

MOH (2020) Zambia Consolidted Guidelines for Treatment and Prevention of HIV Infection, Lusaka: Ministry of Health.

MOH (2022) Zambia Consolidated guidelines for Treatment and Prevention of HIV Infection, Lusaka: Ministry of Health.

Monjok, E., Smesny, A. and Essien, E. J. (2009) 'HIV/AIDS-related stigma and discrimination in Nigeria: review of research studies and future directions for prevention strategies', *Afr J Reprod Health*, 13(3), pp. 21-35. Available at: <u>https://www.ncbi.nlm.nih.gov/pubmed/20690259</u>

Mugavero, M. J., Westfall, A. O., Zinski, A., Davila, J., Drainoni, M. L., Gardner, L. I., Keruly, J. C., Malitz, F., Marks, G., Metsch, L., Wilson, T. E., Giordano, T. P. and Retention in Care Study, G. (2012) 'Measuring retention in HIV care: the elusive gold standard', *J Acquir Immune Defic Syndr*, 61(5), pp. 574-80. DOI: 10.1097/QAI.0b013e318273762f

Mugo, C. W., Shkedy, Z., Mwalili, S., Awoke, T., Braekers, R., Wandede, D. and Mwachari, C. (2022) 'Modelling trends of CD4 counts for patients on antiretroviral therapy (ART): a

comprehensive health care clinic in Nairobi, Kenya', *BMC Infect Dis*, 22(1), pp. 29. DOI: 10.1186/s12879-021-06977-w

Mukamba, N., Sharma, A., Mwamba, C., Nyirenda, H., Foloko, M., Lumbo, K., Christopoulos, K., Simbeza, S., Sikombe, K., Holmes, C. B., Geng, E. H., Sikazwe, I., Bolton-Moore, C. and Beres, L. K. (2022) 'HIV care experiences and health priorities during the first wave of COVID-19: clients' perspectives - a qualitative study in Lusaka, Zambia', *BMC Public Health*, 22(1), pp. 2238. DOI: 10.1186/s12889-022-14493-y

Muri, L., Gamell, A., Ntamatungiro, A. J., Glass, T. R., Luwanda, L. B., Battegay, M., Furrer, H., Hatz, C., Tanner, M., Felger, I., Klimkait, T., Letang, E. and Group, K. S. (2017) 'Development of HIV drug resistance and therapeutic failure in children and adolescents in rural Tanzania: an emerging public health concern', *AIDS*, 31(1), pp. 61-70. DOI: 10.1097/QAD.00000000001273

Murphy, D. A., Wilson, C. M., Durako, S. J., Muenz, L. R. and Belzer, M. (2001) 'Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA', *AIDS Care*, 13(1), pp. 27-40. DOI: 10.1080/09540120020018161

Mutasa-Apollo, T., Shiraishi, R. W., Takarinda, K. C., Dzangare, J., Mugurungi, O., Murungu, J., Abdul-Quader, A. and Woodfill, C. J. (2014) 'Patient retention, clinical outcomes and attrition-associated factors of HIV-infected patients enrolled in Zimbabwe's National Antiretroviral Therapy Programme, 2007-2010', *PLoS One*, 9(1), pp. e86305. DOI: 10.1371/journal.pone.0086305

Muula, A. S. and Kataika, E. (2008) Assessment of equity in the uptake of anti-retrovirals in *Malawi*: University of Cape Town.

Muwanguzi, M., Lugobe, H. M., Ssemwanga, E., Lule, A. P., Atwiine, E., Kirabira, V., Stella, A. K., Ashaba, S. and Rukundo, G. Z. (2021) 'Retention in HIV care and associated factors among youths aged 15-24 years in rural southwestern Uganda', *BMC Public Health*, 21(1), pp. 1489. DOI: 10.1186/s12889-021-11547-5

Mwangi, R., Chandler, C., Nasuwa, F., Mbakilwa, H., Poulsen, A., Bygbjerg, I. C. and Reyburn, H. (2008) 'Perceptions of mothers and hospital staff of paediatric care in 13 public hospitals in

northern Tanzania', *Trans R Soc Trop Med Hyg*, 102(8), pp. 805-10. DOI: 10.1016/j.trstmh.2008.04.033

Nabitaka, V. M., Nawaggi, P., Campbell, J., Conroy, J., Harwell, J., Magambo, K., Middlecote, C., Caldwell, B., Katureebe, C., Namuwenge, N., Atugonza, R., Musoke, A. and Musinguzi, J. (2020) 'High acceptability and viral suppression of patients on Dolutegravir-based first-line regimens in pilot sites in Uganda: A mixed-methods prospective cohort study', *PLoS One*, 15(5), pp. e0232419. DOI: 10.1371/journal.pone.0232419

Nachega, J. B., Hislop, M., Dowdy, D. W., Chaisson, R. E., Regensberg, L. and Maartens, G. (2007) 'Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes', *Ann Intern Med*, 146(8), pp. 564-73. DOI: 10.7326/0003-4819-146-8-200704170-00007

Nachega, J. B., Morroni, C., Zuniga, J. M., Schechter, M., Rockstroh, J., Solomon, S. and Sherer, R. (2012) 'HIV treatment adherence, patient health literacy, and health care providerpatient communication: results from the 2010 AIDS Treatment for Life International Survey', *J Int Assoc Physicians AIDS Care (Chic)*, 11(2), pp. 128-33. DOI: 10.1177/1545109712437244

Nachega, J. B., Mugavero, M. J., Zeier, M., Vitoria, M. and Gallant, J. E. (2011) 'Treatment simplification in HIV-infected adults as a strategy to prevent toxicity, improve adherence, quality of life and decrease healthcare costs', *Patient Prefer Adherence*, 5, pp. 357-67. DOI: 10.2147/PPA.S22771

Nachega, J. B., Uthman, O. A., Peltzer, K., Richardson, L. A., Mills, E. J., Amekudzi, K. and Ouedraogo, A. (2015) 'Association between antiretroviral therapy adherence and employment status: systematic review and meta-analysis', *Bull World Health Organ*, 93(1), pp. 29-41. DOI: 10.2471/BLT.14.138149

Nduaguba, S. O., Soremekun, R. O., Olugbake, O. A. and Barner, J. C. (2017) 'The relationship between patient-related factors and medication adherence among Nigerian patients taking highly active anti-retroviral therapy', *Afr Health Sci*, 17(3), pp. 738-745. DOI: 10.4314/ahs.v17i3.16

Ngarina, M., Popenoe, R., Kilewo, C., Biberfeld, G. and Ekstrom, A. M. (2013) 'Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their

own health: experiences from the Mitra Plus study in Tanzania', *BMC Public Health*, 13, pp. 450. DOI: 10.1186/1471-2458-13-450

Nicol, E., Basera, W., Mukumbang, F. C., Cheyip, M., Mthethwa, S., Lombard, C., Jama, N., Pass, D., Laubscher, R. and Bradshaw, D. (2023) 'Linkage to HIV Care and Early Retention in Care Rates in the Universal Test-and-Treat Era: A Population-based Prospective Study in KwaZulu-Natal, South Africa', *AIDS Behav*, 27(4), pp. 1068-1081. DOI: 10.1007/s10461-022-03844-w

Nozaki, I., Dube, C., Kakimoto, K., Yamada, N. and Simpungwe, J. B. (2011) 'Social factors affecting ART adherence in rural settings in Zambia', *AIDS Care*, 23(7), pp. 831-8. DOI: 10.1080/09540121.2010.542121

Ntombela, N. P., Kharsany, A. B. M., Soogun, A., Yende-Zuma, N., Baxter, C., Kohler, H. P. and McKinnon, L. R. (2022) 'Viral suppression among pregnant adolescents and women living with HIV in rural KwaZulu-Natal, South Africa: a cross sectional study to assess progress towards UNAIDS indicators and Implications for HIV Epidemic Control', *Reprod Health*, 19(1), pp. 116. DOI: 10.1186/s12978-022-01419-5

Nyaboke, R., Ramadhani, H. O., Lascko, T., Awuor, P., Kirui, E., Koech, E., Mutisya, I., Ngunu, C. and Wangusi, R. (2023) 'Factors associated with adherence and viral suppression among patients on second-line antiretroviral therapy in an urban HIV program in Kenya', *SAGE Open Med*, 11, pp. 20503121231162354. DOI: 10.1177/20503121231162354

Nyoni, T. and Okumu, M. (2020) 'COVID-19-Compliant Strategies for Supporting Treatment Adherence Among People Living with HIV in Sub-Saharan Africa', *AIDS Behav*, 24(9), pp. 2473-2476. DOI: 10.1007/s10461-020-02888-0

Okonji, E. F., van Wyk, B., Mukumbang, F. C. and Hughes, G. D. (2021) 'Determinants of viral suppression among adolescents on antiretroviral treatment in Ehlanzeni district, South Africa: a cross-sectional analysis', *AIDS Res Ther*, 18(1), pp. 66. DOI: 10.1186/s12981-021-00391-7

Opoku, S., Sakyi, S. A., Ayisi-Boateng, N. K., Enimil, A. K., Senu, E., Ansah, R. O., Aning, B. D., Ojuang, D. A., Wekesa, D. N., Ahmed, F. O., Okeke, C. B. and Sarfo, A. D. (2022) 'Factors associated with viral suppression and rebound among adult HIV patients on treatment: a

retrospective study in Ghana', AIDS Res Ther, 19(1), pp. 21. DOI: 10.1186/s12981-022-00447-2

Parienti, J. J., Bangsberg, D. R., Verdon, R. and Gardner, E. M. (2009) 'Better adherence with once-daily antiretroviral regimens: a meta-analysis', *Clin Infect Dis*, 48(4), pp. 484-8. DOI: 10.1086/596482

Park, W. B., Choe, P. G., Kim, S. H., Jo, J. H., Bang, J. H., Kim, H. B., Kim, N. J., Oh, M. and Choe, K. W. (2007) 'One-year adherence to clinic visits after highly active antiretroviral therapy: a predictor of clinical progress in HIV patients', *J Intern Med*, 261(3), pp. 268-75. DOI: 10.1111/j.1365-2796.2006.01762.x

Paterson, D. L., Swindells, S., Mohr, J., Brester, M., Vergis, E. N., Squier, C., Wagener, M. M. and Singh, N. (2000) 'Adherence to protease inhibitor therapy and outcomes in patients with HIV infection', *Ann Intern Med*, 133(1), pp. 21-30. DOI: 10.7326/0003-4819-133-1-200007040-00004

Peltzer, K., Friend-du Preez, N., Ramlagan, S. and Anderson, J. (2010) 'Antiretroviral treatment adherence among HIV patients in KwaZulu-Natal, South Africa', *BMC Public Health*, 10, pp. 111. DOI: 10.1186/1471-2458-10-111

Peltzer, K. and Pengpid, S. (2013) 'Socioeconomic factors in adherence to HIV therapy in lowand middle-income countries', *J Health Popul Nutr*; 31(2), pp. 150-70. DOI: 10.3329/jhpn.v31i2.16379

Penn, C., Watermeyer, J. and Evans, M. (2011) 'Why don't patients take their drugs? The role of communication, context and culture in patient adherence and the work of the pharmacist in HIV/AIDS', *Patient Educ Couns*, 83(3), pp. 310-8. DOI: 10.1016/j.pec.2011.02.018

Person, A. K. and Sterling, T. R. (2012) 'Treatment of latent tuberculosis infection in HIV: shorter or longer?', *Curr HIV/AIDS Rep*, 9(3), pp. 259-66. DOI: 10.1007/s11904-012-0120-1

Phiri, M. M., Hensen, B., Schaap, A., Sigande, L., Simuyaba, M., Simwinga, M., Floyd, S., Fidler, S., Hayes, R. and Ayles, H. (2022) 'Adapting community-based sexual and reproductive health services for adolescents and young people aged 15-24 years in response to COVID-19 in Lusaka, Zambia: the implications on the uptake of HIV testing services', *BMC Health Serv Res*, 22(1), pp. 503. DOI: 10.1186/s12913-022-07878-7

POPIA. (2019). Protection of Personal Information, Act 4 of 2019. Available from: <u>http://www.gov.za/sites/www.gov.za/files/37067\_26-</u> 11 Act4of2013ProtectionOfPersonalInfor correct.pdf

Pry, J. M., Sikombe, K., Mody, A., Iyer, S., Mutale, J., Vlahakis, N., Savory, T., Wa Mwanza, M., Mweebo, K., Mwila, A., Mwale, C., Mukumbwa-Mwenechanya, M., Kerkhoff, A. D., Sikazwe, I., Bolton Moore, C., Mwamba, D., Geng, E. H. and Herce, M. E. (2022) 'Mitigating the effects of COVID-19 on HIV treatment and care in Lusaka, Zambia: a before-after cohort study using mixed effects regression', *BMJ Glob Health*, 7(1). DOI: 10.1136/bmjgh-2021-007312

Rahman, M. S. (2016) 'The Advantages and Disadvantages of Using Qualitative and Quantitative Approaches and Methods in Language "Testing and Assessment" Research: A Literature Review', *Journal of Education and Learning*, 6(1). DOI: 10.5539/jel.v6n1p102

Rangarajan, S., Donn, J. C., Giang le, T., Bui, D. D., Hung Nguyen, H., Tou, P. B., Danh, T. T., Tran, N. B., Nguyen, D. A., Hoang Nguyen, B. T., Doan, V. T., Nguyen, N. Q., Pham, V. P., Dao, D. G., Chen, M., Zeng, Y., Tieu, T. T., Tran, M. H., Le, T. H., Hoang, X. C. and West, G. (2016) 'Factors associated with HIV viral load suppression on antiretroviral therapy in Vietnam', *J Virus Erad*, 2(2), pp. 94-101. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27482442

Rao, A. G., Sutton, S. S., Bennet, C. and Hardin, J. (2013) 'Impact of Highly Active Antiretroviral Therapy (HAART) Regimen on Adherence and Risk of Hospitalization in Veterans with HIV/AIDS', *Value in Health*, 16(7), pp. a341. DOI: 10.1016/j.jval.2013.08.112

Rao, D., Kekwaletswe, T. C., Hosek, S., Martinez, J. and Rodriguez, F. (2007) 'Stigma and social barriers to medication adherence with urban youth living with HIV', *AIDS Care*, 19(1), pp. 28-33. DOI: 10.1080/09540120600652303

Robson, C., & McCartan, K. (2016). Real World Research (4th ed.). Wiley

Rogers, A. A., Halle, E. G., Egbe , O. T., Nsah, A. N., Anastase, D., Assob, N. J. and Adebola, A. (2021) 'Determinants of retention in HIV antiretroviral treatment (ART) in the Cameroon International epidemiology', *Pan Afr Med J*, (129). DOI: 0.11604/pamj.2021.40.129.22642

Rosa, M. C., Lobato, R. C., Goncalves, C. V., Silva, N. M., Barral, M. F., Martinez, A. M. and Hora, V. P. (2015) 'Evaluation of factors associated with vertical HIV-1 transmission', *J Pediatr* (*Rio J*), 91(6), pp. 523-8. DOI: 10.1016/j.jped.2014.12.005

Rosen, S., Fox, M. P. and Gill, C. J. (2007) 'Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review', *PLoS Med*, 4(10), pp. e298. DOI: 10.1371/journal.pmed.0040298

Ross-Degnan, D., Pierre-Jacques, M., Zhang, F., Tadeg, H., Gitau, L., Ntaganira, J., Balikuddembe, R., Chalker, J., Wagner, A. K. and Inrud, I. A. A. (2010) 'Measuring adherence to antiretroviral treatment in resource-poor settings: the clinical validity of key indicators', *BMC Health Serv Res*, 10, pp. 42. DOI: 10.1186/1472-6963-10-42

Sanjobo, N., Frich, J. C. and Fretheim, A. (2008) 'Barriers and facilitators to patients' adherence to antiretroviral treatment in Zambia: a qualitative study', *SAHARA J*, 5(3), pp. 136-43. DOI: 10.1080/17290376.2008.9724912

Santos, V. D. F., Pedrosa, S. C., Aquino, P. S., Lima, I. C. V., Cunha, G. H. D. and Galvao, M. T. G. (2018) 'Social support of people with HIV/AIDS: the Social Determinants of Health Model', *Rev Bras Enferm*, 71(suppl 1), pp. 625-630. DOI: 10.1590/0034-7167-2017-0346

Sauceda, J. A., Neilands, T. B., Johnson, M. O. and Saberi, P. (2018) 'An update on the Barriers to Adherence and a Definition of Self-Report Non-adherence Given Advancements in Antiretroviral Therapy (ART)', *AIDS Behav*, 22(3), pp. 939-947. DOI: 10.1007/s10461-017-1759-9

Scheurer, D., Choudhry, N., Swanton, K. A., Matlin, O. and Shrank, W. (2012) 'Association between different types of social support and medication adherence', *Am J Manag Care*, 18(12), pp. e461-7. Available at: <u>https://www.ncbi.nlm.nih.gov/pubmed/23286676</u>

Sekaran, U., & Bougie, R. (2010). Research methods for business: A skill-building approach (5th ed.). Haddington: John Wiley & Sons.

Shah, G. H., Etheredge, G. D., Nkuta, L. M., Waterfield, K. C., Ikhile, O., Ditekemena, J. and Bernard, B. N. B. (2022) 'Factors Associated with Retention of HIV Patients on Antiretroviral Therapy in Care: Evidence from Outpatient Clinics in Two Provinces of the Democratic Republic of the Congo (DRC)', *Trop Med Infect Dis*, 7(9). DOI: 10.3390/tropicalmed7090229

Shigayeva, A., Gcwensa, N., Ndlovu, C. D., Ntumase, N., Sabela, S., Ohler, L., Trivino-Duran, L., Kamara, E. F., Hlophe, K., Isaakidis, P. and Van Cutsem, G. (2022) 'Retention on ART and viral suppression among patients in alternative models of differentiated HIV service delivery in KwaZulu-Natal, South Africa', *PLOS Glob Public Health*, 2(12), pp. e0000336. DOI: 10.1371/journal.pgph.0000336

Shigdel, R., Klouman, E., Bhandari, A. and Ahmed, L. A. (2014) 'Factors associated with adherence to antiretroviral therapy in HIV-infected patients in Kathmandu District, Nepal', *HIV AIDS (Auckl)*, 6, pp. 109-16. DOI: 10.2147/HIV.S55816

Simoni, J. M., Kurth, A. E., Pearson, C. R., Pantalone, D. W., Merrill, J. O. and Frick, P. A. (2006) 'Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management', *AIDS Behav*, 10(3), pp. 227-45. DOI: 10.1007/s10461-006-9078-6

Skovdal, M., Campbell, C., Nhongo, K., Nyamukapa, C. and Gregson, S. (2011) 'Contextual and psychosocial influences on antiretroviral therapy adherence in rural Zimbabwe: towards a systematic framework for programme planners', *Int J Health Plann Manage*, 26(3), pp. 296-318. DOI: 10.1002/hpm.1082

Somi, N., Dear, N., Reed, D., Parikh, A., Lwilla, A., Bahemana, E., Khamadi, S., Iroezindu, M., Kibuuka, H., Maswai, J., Crowell, T. A., Owuoth, J., Maganga, L., Polyak, C., Ake, J., Esber, A. and Group, A. S. (2021) 'Perceived satisfaction with HIV care and its association with adherence to antiretroviral therapy and viral suppression in the African Cohort Study', *AIDS Res Ther*, 18(1), pp. 89. DOI: 10.1186/s12981-021-00414-3

Spies, G., Denckla, C. A., Mall, S., Levin, J., Seedat, S., Nakasujja, N. and Kinyanda, E. (2019) 'The relationship between cognitive change and physical health and behavioural outcomes in a Ugandan cohort of adults living with HIV - a longitudinal study', *AIDS Care*, 31(7), pp. 803-808. DOI: 10.1080/09540121.2018.1545987

Staveteig, S., Wang, S., Head, K. S., Bradley, E. K. S. and Nybro, E. (2013) *Demographic patterns of HIV testing uptake in sub-Saharan Africa*. *DHS Comparative Reports No. 30*. Available at: <u>http://dhsprogram.com/pubs/pdf/CR30/CR30.pdf</u>.

Steiner, F. J. and Prochazka, V. A. 'The assessment of refill compliance using pharmacy records: Methods, validity, and applications', *Journal of Clinical Epidemiology*, 50(1), pp. 105-116. DOI: <u>https://doi.org/10.1016/S0895-4356(96)00268-5</u>

Stricker, S. M., Fox, K. A., Baggaley, R., Negussie, E., de Pee, S., Grede, N. and Bloem, M.
W. (2014) 'Retention in care and adherence to ART are critical elements of HIV care interventions', *AIDS Behav*, 18 Suppl 5, pp. S465-75. DOI: 10.1007/s10461-013-0598-6

Taherdoost (2016) 'Validity and Reliability of the Research Instrument How to Test the Validation of a Questionnaire Survey in a Research.', *International Journal of Academic Research in Management*, 5(3), pp. 28-36

Takarinda, K. C., Harries, A. D., Shiraishi, R. W., Mutasa-Apollo, T., Abdul-Quader, A. and Mugurungi, O. (2015) 'Gender-related differences in outcomes and attrition on antiretroviral treatment among an HIV-infected patient cohort in Zimbabwe: 2007-2010', *Int J Infect Dis*, 30, pp. 98-105. DOI: 10.1016/j.ijid.2014.11.009

Tanyi, W. N., Gachuno, O., Odero, T., Farquhar, C., Kimosop, D. and Mayi, A. (2021) 'Factors affecting adherence to antiretroviral therapy among children and adolescents living with HIV in the Mbita Sub-County Hospital, Homa Bay- Kenya', *Afr Health Sci*, 21(Suppl), pp. 18-24. DOI: 10.4314/ahs.v21i1.4S

Tegegne, A. S. (2021) 'Socio-Demographic, Economic and Clinical Predictors for HAART Adherence Competence in HIV-Positive Adults at Felege Hiwot Teaching and Specialized Hospital, North West Ethiopia', *HIV AIDS (Auckl)*, 13, pp. 749-758. DOI: 10.2147/HIV.S320170

Toossi, Z., Mayanja-Kizza, H., Hirsch, C. S., Edmonds, K. L., Spahlinger, T., Hom, D. L., Aung, H., Mugyenyi, P., Ellner, J. J. and Whalen, C. W. (2001) 'Impact of tuberculosis (TB) on HIV-1 activity in dually infected patients', *Clin Exp Immunol*, 123(2), pp. 233-8. DOI: 10.1046/j.1365-2249.2001.01401.x

Tripathi, A., Youmans, E., Gibson, J. J. and Duffus, W. A. (2011) 'The impact of retention in early HIV medical care on viro-immunological parameters and survival: a statewide study', *AIDS Res Hum Retroviruses*, 27(7), pp. 751-8. DOI: 10.1089/AID.2010.0268

Tsague, L., Koulla, S. S., Kenfak, A., Kouanfack, C., Tejiokem, M., Abong, T., Mbangue, M., Mapoure, Y. N., Essomba, C., Mosoko, J., Pouillot, R., Menyeng, L., Epee, H., Tchuani, C., Zoung-Kanyi, A. C., Bella, L. A. and Zekeng, L. (2008) 'Determinants of retention in care in an antiretroviral therapy (ART) program in urban Cameroon, 2003-2005', *Pan Afr Med J*, 1, pp. 2. Available at: <u>https://www.ncbi.nlm.nih.gov/pubmed/21532891</u>

Umeokonkwo, C. D., Onoka, C. A., Agu, P. A., Ossai, E. N., Balogun, M. S. and Ogbonnaya, L. U. (2019) 'Retention in care and adherence to HIV and AIDS treatment in Anambra State Nigeria', *BMC Infect Dis*, 19(1), pp. 654. DOI: 10.1186/s12879-019-4293-8

UNAIDS (2015) 'Understanding Fast-Track Targets. Accelerating action to end the AIDS epidemic by 2030. Available: '. Available at: <u>https://www.unaids.org/sites/default/files/media\_asset/201506\_JC2743\_Understanding\_FastTrack\_en.pdf</u>. (Accessed 22.2.2022).

UNAIDS (2022) 'Global HIV Statistics'. Available at: <u>https://www.unaids.org/sites/default/files/media\_asset/UNAIDS\_FactSheet\_en.pdf</u> (Accessed 22.2.2022).

Urquhart, J. (1996) 'Patient non-compliance with drug regimens: measurement, clinical correlates, economic impact', *Eur Heart J*, 17 Suppl A, pp. 8-15. DOI: 10.1093/eurheartj/17.suppl\_a.8

Viswanathan, S., Detels, R., Mehta, S. H., Macatangay, B. J., Kirk, G. D. and Jacobson, L. P. (2015) 'Level of adherence and HIV RNA suppression in the current era of highly active antiretroviral therapy (HAART)', *AIDS Behav*, 19(4), pp. 601-11. DOI: 10.1007/s10461-014-0927-4

Wainberg, M. A. and Friedland, G. (1998) 'Public health implications of antiretroviral therapy and HIV drug resistance', *JAMA*, 279(24), pp. 1977-83. DOI: 10.1001/jama.279.24.1977

Wakooko, P., Gavamukulya, Y. and Wandabwa, J. N. (2020) 'Viral load Suppression and Associated Factors among HIV Patients on Antiretroviral Treatment in Bulambuli District, Eastern Uganda: A Retrospective Cohort Study', *Infect Dis (Auckl)*, 13, pp. 1178633720970632. DOI: 10.1177/1178633720970632

Wang, X. and Cheng, Z. (2020) 'Cross-Sectional Studies: Strengths, Weaknesses, and Recommendations', *Chest*, 158(1S), pp. S65-S71. DOI: 10.1016/j.chest.2020.03.012

Wardhani, S. F. and Yona, S. (2021) 'Spousal intimacy, type of antiretroviral drug and antiretroviral therapy adherence among HIV patients in Bandung, Indonesia', *J Public Health Res*, 10(s1). DOI: 10.4081/jphr.2021.2336

Wasti, S. P., Simkhada, P., Randall, J., Freeman, J. V. and van Teijlingen, E. (2012) 'Factors influencing adherence to antiretroviral treatment in Nepal: a mixed-methods study', *PLoS One*, 7(5), pp. e35547. DOI: 10.1371/journal.pone.0035547

Weinberg, J. L. and Kovarik, C. L. (2010) 'The WHO Clinical Staging System for HIV/AIDS', *Virtual Mentor*, 12(3), pp. 202-6. DOI: 10.1001/virtualmentor.2010.12.3.cprl1-1003

Weiser, S., Wolfe, W., Bangsberg, D., Thior, I., Gilbert, P., Makhema, J., Kebaabetswe, P., Dickenson, D., Mompati, K., Essex, M. and Marlink, R. (2003) 'Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana', *J Acquir Immune Defic Syndr*, 34(3), pp. 281-8. DOI: 10.1097/00126334-200311010-00004

Weiser, S. D., Tuller, D. M., Frongillo, E. A., Senkungu, J., Mukiibi, N. and Bangsberg, D. R. (2010) 'Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda', *PLoS One*, 5(4), pp. e10340. DOI: 10.1371/journal.pone.0010340

WHO (2017) Treat All: Policy adoption and Implementation Status in Countries. HIV treatment and Care. Available at: <u>http://apps.who.int/iris/bitstream/10665/258538/1/WHO-HIV-2017.35-eng.pdf?ua=1</u>.

WHO (2018a) Dolutegravir (DTG) and the fixed dose combination (FDC) of tenofovir/lamivudine/dolutegravir (TLD).

WHO (2018b) TB burden report. Available at: https://apps.who.int/iris/handle/10665/274453.

Wyk, B. V. and Mayman, Y. (2022) 'Impact of COVID-19 pandemic in adolescents on HIV treatment', *Pan Afr Med J*, 42, pp. 120. DOI: 10.11604/pamj.2022.42.120.33774

Yehia, B. R., Rebeiro, P., Althoff, K. N., Agwu, A. L., Horberg, M. A., Samji, H., Napravnik, S., Mayer, K., Tedaldi, E., Silverberg, M. J., Thorne, J. E., Burchell, A. N., Rourke, S. B., Rachlis, A., Mayor, A., Gill, M. J., Zinski, A., Ohl, M., Anastos, K., Abraham, A. G., Kitahata,

M. M., Moore, R. D., Gebo, K. A., North American, A. C. C. o. R. and Design (2015) 'Impact of age on retention in care and viral suppression', *J Acquir Immune Defic Syndr*, 68(4), pp. 413-9. DOI: 10.1097/QAI.000000000000489

Zanoni, B. C. and Mayer, K. H. (2014) 'The adolescent and young adult HIV cascade of care in the United States: exaggerated health disparities', *AIDS Patient Care STDS*, 28(3), pp. 128-35. DOI: 10.1089/apc.2013.0345

Zanoni, B. C., Phungula, T., Zanoni, H. M., France, H. and Feeney, M. E. (2011) 'Impact of tuberculosis cotreatment on viral suppression rates among HIV-positive children initiating HAART', *AIDS*, 25(1), pp. 49-55. DOI: 10.1097/QAD.0b013e32833f9e04

Zhang, L., Li, X., Lin, Z., Jacques-Tiura, A. J., Xu, J., Zhou, Y., Qiao, S., Shen, Z. and Stanton, B. (2016) 'Side effects, adherence self-efficacy, and adherence to antiretroviral treatment: a mediation analysis in a Chinese sample', *AIDS Care*, 28(7), pp. 919-26. DOI: 10.1080/09540121.2015.1124984

Zikargae, M. H. (2020) 'COVID-19 in Ethiopia: Assessment of How the Ethiopian Government has Executed Administrative Actions and Managed Risk Communications and Community Engagement', *Risk Manag Healthc Policy*, 13, pp. 2803-2810. DOI: 10.2147/RMHP.S278234



UNIVERSITY of the WESTERN CAPE

#### **APPENDICES**

# **APPENDIX 1: UWC ethics clearance letter**

UNIVERSITY of the WESTERN CAPE	<b>YEARS</b> of hope, action Schnowledge
29 November 2022	
Ms C Chilumwaya School of Public Health <b>Faculty of Community and Health</b>	Sciences
BMREC Reference Number:	BM22/9/6
Project Title:	Antiretroviral therapy adherence among People Living with HIV accessing services at a zonal primary health care facility in Livingstone, Zambia during the COVID-19 pandemic
Approval Period:	29 November 2022 – 28 November 2025
I hereby certify that the Biomedical	Science Research Ethics Committee of the University

of the Western Cape approved the scientific methodology and ethics of the above mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via: https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

The Committee must be informed of any serious adverse event and/or termination of the study.

pres

Ms Patricia Josias Research Ethics Committee Officer University of the Western Cape

NHREC Registration Number: BMREC-130416-050

Director: Research Development University of the Western Cape Private Bag X 17 Bellville 7535 Republic of South Africa Tel: +27 21 959 4111 Email: research-ethics@uwc.ac.za

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

#### **APPENDIX 2: MUSOMHS ethics clearance letter**



Mulungushi University

School of Medicine and Health Sciences

#### Ethics Review Committee

IRB: 00012281 FWA: 0002888 Email: somhsethics@mu.ac.zm

Ref. No.: SMHS-MU3-2022-14

30th August 2022

Cynthia Chilumwaya

University of the Western Cape

South Africa Dear Cynthia,

RE: ETHICAL CLEARANCE OF THE STUDY PROTOCOL

Reference is made to your protocol entitled, "Antiretroviral therapy adherence among people living with HIV accessing services at a zonal primary health care facility in Livingstone, Zambia during the covid-19 pandemic" that was submitted on 28<sup>th</sup> August 2022.

On behalf of the Research Ethics Committee (REC) Chairperson, I wish to inform you that your protocol has been successfully reviewed and according to the reviewer's recommendations your protocol has been granted Ethical clearance based on the following conditions:

Should there be need to modify or amend the approved protocol, you are required to notify the REC and submit protocol amendments for approval by quoting your REC reference number. You are further required to submit progress reports to the REC twice a year and a final report at the end of your study. You must report serious adverse events related to the conduct of the study and any unforeseen circumstances to the REC.

You are now required to submit your protocol to National Health Research Authority (NHRA) for authorization following the link: <u>https://www.nhra.org.zm/</u>

This approval is valid for a period 30th August 2022 to 30th August 2023.

The Committee wishes you success in the execution of your study.

. .

Yours sincerely,

MULUNGUSHI UNIVERSITY - SOMHS \_ RESEARCH ETHICS COMMITTEE

Warren Chanda

SECRETARY - MUSOMHS\_REC

Cc: Chairperson – MUSOMHS\_REC

### **APPENDIX 3: NHRA clearance letter**



#### NATIONAL HEALTH RESEARCH AUTHORITY Paediatric Centre of Excellence, University Teaching Hospital, P.O. Box 30075, LUSAKA Chalala Office Lot No. 18961/M, Off Kasama Road, P.O. Box 30075, LUSAKA Tell: +260211 250309 | Email: znhrasec@nhra.org.zm | www.nhra.org.zm

Ref No: NHRA0000001/04/09/2022

Date: 4<sup>th</sup> September, 2022

The Principal Investigator, Cynthia Chilumwaya, University of Western Cape, Lusaka, Zambia

Dear Ms. Chilumwaya,

Re: Request for Authority to Conduct Research

The National Health Research Authority is in receipt of your request for ethical clearance and authority to conduct research titled "Antiretroviral Therapy Adherence among People Living with HIV Accessing Services at a Zonal Primary Health Care Facility in Livingstone, Zambia during the Covid-19 Pandemic".

I wish to inform you that following submission of your request to the Authority, our review of the same and in view of the ethical clearance, this study has been approved on condition that:

- 1. The relevant Provincial and District Medical Officers where the study is being conducted are fully appraised;
- Progress updates are provided to NHRA quarterly from the date of commencement of the study;
- The final study report is cleared by the NHRA before any publication or dissemination within or outside the country;
- 4. After clearance for publication or dissemination by the NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University leadership, and all key respondents.

U.

Yours sincerely,

Prof. Godfrey Biemba, Director/CEO, National Health Research Authority

#### **APPENDIX 4: Permission letter from Livingstone DHO**

The District Health Director Livingstone District Health Office Livingstone

23rd August 2022.

# RE: REQUEST TO USE SECONDARY DATA FROM THE ELECTRONIC MEDICAL RECORD FOR MY RESEARCH

Dear Sir,

I am a student currently pursuing a master's in public health (MPH) with the University of the Western Cape (UWC) and currently preparing for my thesis. My topic is: "Antiretroviral therapy adherence among People Living with HIV accessing services at a zonal primary health care facility in Livingstone, Zambia during the COVID-19 pandemic". This study will be conducted at Mahatma Gandhi clinic using secondary data form the electronic medical record (SmartCare).

Based on the above description, I write to request for permission to use the secondary data for the purpose of my thesis. To ensure patient anonymity, no patient names or identifiers will be recorded in any study material. All records used during and after the study will be stored in password protected storage devices only accessible to the researcher. Ethical clearance from all relevant bodies will be obtained prior to conducting this research and will be availed to your office.

Yours Sincerely, dra-Edun Days Cynthia Chilumwaya 2.5708/22 No Ubjeetinis .08 60796 HEALTH DIRECTOR ccoLIVINGSTON



PE

# **EDITING CERTIFICATE**

16 May 2023

TO WHOM IT MAY CONCERN

**DECLARATION: Editing of Mini-thesis** 

I hereby declare that the Master in Public Health mini-thesis of **Cynthia Chilumwaya** entitled "ANTIRETROVIRAL THERAPY ADHERENCE AMONG PEOPLE LIVING WITH HIV ACCESSING SERVICES AT A PRIMARY HEALTH CARE FACILITY IN LIVINGSTONE, ZAMBIA, DURING THE COVID-19 PANDEMIC" has been edited. It is the responsibility of the student to address any comments from the editor or supervisor. The editor shall not be responsible for any subsequent additions or deletions made by the student in their document. Additionally, it is the final responsibility of the student to make sure of the correctness of the mini-thesis.



# Khomotso Bopape

Full Member of the Professional Editors' Guild



Let's Edit is a Level 1 EME B-BBEE Contributor (Procurement Recognition Level = 135%)

Address: 570 Fehrsen Street, Brooklyn Bridge Office Park, Brooklyn, Pretoria, 0181 Tel No.: 012 433 6584, Fax No.: 086 267 2164 and Email Address: editor@letsedit.co.za